WEST Search History

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DATE: Tuesday, March 06, 2007

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,EPAB; PLUR=YES; OP=ADJ	
☐	L40	L39 and antisense	0
☐	L39	L38 and l37	4
☐	L38	l35.ab. or l35.clm.	16
☐	L37	L36 not @ay>2001	87
☐	L36	L35 and (cancer$ or tumor$ or neoplas$)	207
☐	L35	ESP-2 or HED-2 or Zyxin or Zyxin-2	220
☐	L34	L33 not @ay>2001	4
☐	L33	L3 and L21	79
☐	L32	L31 and L26	4
☐	L31	L30 and L24	802
☐	L30	stabil$	1165863
☐	L29	L19 and L24	23
☐	L28	L26 and L21	4
☐	L27	L26 abd k21	0
☐	L26	L16.ab.	333
☐	L25	s L17.ab.	1
☐	L24	L21 and L16	919
☐	L23	L21 and L19	23
☐	L22	L21 and L20	25
☐	L21	ewing$ NEAR2 sarcoma	2520
☐	L20	zyxin	203
☐	L19	cofilin	261
☐	L18	L17 and L14	5
☐	L17	actin	30701
☐	L16	actin	30701
☐	L15	L14 and L13	3
☐	L14	(auclair or amsellem or hervy or subra).in.	397
☐	L13	L12 or L11 or L10	25539
☐	L12	(435/7.23)![CCLS]	3836
☐	L11	(424/93.21)![CCLS]	2119
☐	L10	(514/12 |514/44 |514/9)![CCLS]	20573

☐	L9	L8 AND L3	1
☐	L8	20040191230.pn.	1
☐	L7	L5 not @ay>2001	4
☐	L6	L5 not @py>2001	0
☐	L5	L4 and sarcoma	111
☐	L4	L3 and ewing$	111
☐	L3	jasplakinolide	276
☐	L2	L1 and ewing$	1
☐	L1	dolastatin 11	13

END OF SEARCH HISTORY

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	6.33	78.66

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-10.92

STN INTERNATIONAL LOGOFF AT 10:25:55 ON 06 MAR 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1642BJF

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 8	JAN 30	Saved answer limit increased
NEWS 9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 14	FEB 28	TOXCENTER reloaded with enhancements
NEWS 15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 16	MAR 01	INSPEC reloaded and enhanced
NEWS 17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 18	MAR 08	X.25 communication option no longer available after June 2006
NEWS 19	MAR 22	EMBASE is now updated on a daily basis
NEWS 20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS 22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS 23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS 25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

NEWS EXPRESS	FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT http://download.cas.org/express/v8.0-Discover/
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:41:45 ON 17 APR 2006

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:41:55 ON 17 APR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 16 APR 2006 HIGHEST RN 880543-27-1
DICTIONARY FILE UPDATES: 16 APR 2006 HIGHEST RN 880543-27-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

```
**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************
```

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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=> E "DOLASTATIN"/CN 25
E1            1     DOLASETRON MESYLATE/CN
E2            1     DOLASTANE/CN
E3            0 --> DOLASTATIN/CN
E4            1     DOLASTATIN 1/CN
E5            1     DOLASTATIN 10/CN
E6            1     DOLASTATIN 11/CN
E7            1     DOLASTATIN 12/CN
E8            1     DOLASTATIN 13/CN
E9            1     DOLASTATIN 13,
4-(3-AMINO-3,4-DIHYDRO-2-OXO-A-(PHENYLMETHYL)-1(2H)-PYRIDINEACETIC ACID)-/CN
E10           1     DOLASTATIN 13,
4-(3-AMINO-3,4-DIHYDRO-6-HYDROXY-2-OXO-A-(PHENYLMETHYL)-1(2H)-PYRIDINEACETIC
ACID)-/CN
E11           1     DOLASTATIN 14/CN
E12           1     DOLASTATIN 15/CN
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E13          1      DOLASTATIN 16/CN
E14          1      DOLASTATIN 17/CN
E15          1      DOLASTATIN 17 (DOLABELLA AURICULARIA)/CN
E16          1      DOLASTATIN 18/CN
E17          1      DOLASTATIN 19/CN
E18          1      DOLASTATIN 2/CN
E19          1      DOLASTATIN 3/CN
E20          1      DOLASTATIN 4/CN
E21          1      DOLASTATIN 5/CN
E22          1      DOLASTATIN 6/CN
E23          1      DOLASTATIN 7/CN
E24          1      DOLASTATIN 8/CN
E25          1      DOLASTATIN 9/CN

=> S E6
L1           1 "DOLASTATIN 11"/CN

=> DIS L1 1 SQIDE
THE ESTIMATED COST FOR THIS REQUEST IS 6.36 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   111517-68-1  REGISTRY
CN   Cyclo[L-alanyl-(2S,3R)-3-amino-2-methylpentanoyl-(2S,3S)-2-hydroxy-3-
     methylpentanoylglycyl-N-methyl-L-leucylglycyl-N-methyl-L-valyl-N,O-
     dimethyl-L-tyrosyl-(4S)-4-amino-2,2-dimethyl-3-oxopentanoyl] (9CI)  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   1-Oxa-4,7,10,13,16,19,24,27-octaazacyclotriacontane, cyclic peptide deriv.
CN   Dolastatin 11
OTHER NAMES:
CN   NSC 606195
FS   PROTEIN SEQUENCE; STEREOSEARCH
SQL  8
NTE  modified (modifications unspecified)
```

type	------ location ------		description
bridge	Gly-1	- Oaa-8	covalent bridge
uncommon	Oaa-6	-	-
uncommon	Oaa-8	-	-

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SEQ      1 GLGVYXAX
MF   C50 H80 N8 O12
SR   CA
LC   STN Files:   BEILSTEIN*, BIOSIS, CA, CAPLUS, NAPRALERT, TOXCENTER,
       USPATFULL
         (*File contains numerically searchable property data)
DT.CA  CAplus document type:  Dissertation; Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); PROC (Process); PRP
       (Properties); USES (Uses)
RL.NP  Roles from non-patents:  BIOL (Biological study); PREP (Preparation);
       PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents:  PREP
       (Preparation); PRP (Properties)
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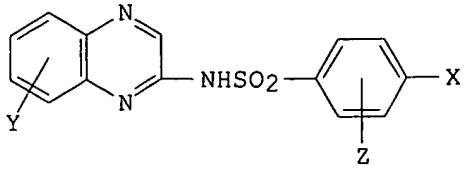

I

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

22 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
22 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> DIS L1 1 SQIDE
THE ESTIMATED COST FOR THIS REQUEST IS 6.36 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:N
REQUEST CANCELED

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	12.00	12.21

FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 17 Apr 2006 VOL 144 ISS 17
FILE LAST UPDATED: 16 Apr 2006 (20060416/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s actin
49670 ACTIN
30327 ACTINS
L2 52669 ACTIN
(ACTIN OR ACTINS)

=> s cofilin
775 COFILIN
232 COFILINS
L3 812 COFILIN
(COFILIN OR COFILINS)

=> s antag? or inhibit?
281605 ANTAG?
1822219 INHIBIT?
L4 1968300 ANTAG? OR INHIBIT?

=> s l4 (l) l3
L5 222 L4 (L) L3

=> s ewing?
L6 1659 EWING?

```
=> s l6 and l5
L7            1 L6 AND L5

=> d ibib

L7   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2002:977858  CAPLUS
DOCUMENT NUMBER:          138:52333
TITLE:                    Pharmaceutical composition for diagnosis, prevention
                          or treatment of a tumorous state, comprising a
                          modulator of the actin polymerization state
INVENTOR(S):              Auclair, Christian; Amsellem, Valerie; Hervy, Martial;
                          Subra, Frederic
PATENT ASSIGNEE(S):       Bioalliance Pharma, Fr.; Ecole Normale Superieure De
                          Cachan; Institut Gustave Roussy-IGR; Centre National
                          de la Recherche Scientifique CNRS
SOURCE:                   PCT Int. Appl., 68 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.            KIND   DATE        APPLICATION NO.          DATE
     ---------------       ----   --------    --------------------     --------
     WO 2002102846          A2    20021227    WO 2002-FR2106           20020618
     WO 2002102846          A3    20040422
     WO 2002102846          B1    20040603
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
            GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
            GN, GQ, GW, ML, MR, NE, SN, TD, TG
     FR 2825928             A1    20021220    FR 2001-7976             20010618
     FR 2825928             B1    20040402
     CA 2450845             AA    20021227    CA 2002-2450845          20020618
     EP 1432732             A2    20040630    EP 2002-745538           20020618
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2005504521          T2    20050217    JP 2003-506318           20020618
     US 2004191230          A1    20040930    US 2003-740266           20031218
PRIORITY APPLN. INFO.:                         FR 2001-7976         A   20010618
                                               WO 2002-FR2106       W   20020618


=> s l1
L8           22 L1

=> s l8 and l6
L9            0 L8 AND L6

=> s zyxin
            219 ZYXIN
             28 ZYXINS
L10         224 ZYXIN
                (ZYXIN OR ZYXINS)

=> s l10 and l6
L11           3 L10 AND L6
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=> d ibib 1-3

L11 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:184733 CAPLUS
DOCUMENT NUMBER: 142:371546
TITLE: The actin cytoskeleton-associated protein zyxin acts as a tumor suppressor in Ewing tumor cells
AUTHOR(S): Amsellem, Valerie; Kryszke, Marie-Helene; Hervy, Martial; Subra, Frederic; Athman, Rafika; Leh, Herve; Brachet-Ducos, Corinne; Auclair, Christian
CORPORATE SOURCE: CNRS UMR 8113, Laboratoire de Biotechnologie et Pharmacologie genetique appliquee, Ecole Normale Superieure de Cachan, Cachan, 94230, Fr.
SOURCE: Experimental Cell Research (2005), 304(2), 443-456
CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:583223 CAPLUS
DOCUMENT NUMBER: 141:188806
TITLE: Molecular mechanisms of CD99-induced caspase-independent cell death and cell-cell adhesion in Ewing's sarcoma cells: actin and zyxin as key intracellular mediators
AUTHOR(S): Cerisano, Vanessa; Aalto, Yan; Perdichizzi, Stefania; Bernard, Ghislaine; Manara, Maria Cristina; Benini, Stefania; Cenacchi, Giovanna; Preda, Paola; Lattanzi, Giovanna; Nagy, Balint; Knuutila, Sakari; Colombo, Mario Paolo; Bernard, Alain; Picci, Piero; Scotlandi, Katia
CORPORATE SOURCE: Laboratorio di Ricerca Oncologica, Istituti Ortopedici Rizzoli, Bologna, 40136, Italy
SOURCE: Oncogene (2004), 23(33), 5664-5674
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:977858 CAPLUS
DOCUMENT NUMBER: 138:52333
TITLE: Pharmaceutical composition for diagnosis, prevention or treatment of a tumorous state, comprising a modulator of the actin polymerization state
INVENTOR(S): Auclair, Christian; Amsellem, Valerie; Hervy, Martial; Subra, Frederic
PATENT ASSIGNEE(S): Bioalliance Pharma, Fr.; Ecole Normale Superieure De Cachan; Institut Gustave Roussy-IGR; Centre National de la Recherche Scientifique CNRS
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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     ---------------      ----   --------    --------------------   --------
     WO 2002102846         A2    20021227    WO 2002-FR2106         20020618
     WO 2002102846         A3    20040422
     WO 2002102846         B1    20040603
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
             GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
             GN, GQ, GW, ML, MR, NE, SN, TD, TG
     FR 2825928            A1    20021220    FR 2001-7976           20010618
     FR 2825928            B1    20040402
     CA 2450845            AA    20021227    CA 2002-2450845        20020618
     EP 1432732            A2    20040630    EP 2002-745538         20020618
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2005504521         T2    20050217    JP 2003-506318         20020618
     US 2004191230         A1    20040930    US 2003-740266         20031218
PRIORITY APPLN. INFO.:                       FR 2001-7976       A   20010618
                                             WO 2002-FR2106     W   20020618


=> d his

     (FILE 'HOME' ENTERED AT 14:41:45 ON 17 APR 2006)

     FILE 'REGISTRY' ENTERED AT 14:41:55 ON 17 APR 2006
               E "DOLASTATIN"/CN 25
L1             1 S E6

     FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006
L2         52669 S ACTIN
L3           812 S COFILIN
L4       1968300 S ANTAG? OR INHIBIT?
L5           222 S L4 (L) L3
L6          1659 S EWING?
L7             1 S L6 AND L5
L8            22 S L1
L9             0 S L8 AND L6
L10          224 S ZYXIN
L11            3 S L10 AND L6

=> s l3 and l6
L12            6 L3 AND L6

=> s l12 and l4
L13            4 L12 AND L4

=> d ibib 1-4

L13  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:248644  CAPLUS
DOCUMENT NUMBER:          142:274057
TITLE:                    Sequences of human schizophrenia related genes and use
                          for diagnosis, prognosis and therapy
INVENTOR(S):              Liew, Choong-chin
PATENT ASSIGNEE(S):       Chondrogene Limited, Can.
SOURCE:                   U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S.
                          Ser. No. 802,875.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
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LANGUAGE: English
FAMILY ACC. NUM. COUNT: 47
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004241727	A1	20041202	US 2004-812731		20040330
US 2004014059	A1	20040122	US 2002-268730		20021009
US 2005191637	A1	20050901	US 2004-803737		20040318
US 2005196762	A1	20050908	US 2004-803759		20040318
US 2005196763	A1	20050908	US 2004-803857		20040318
US 2005196764	A1	20050908	US 2004-803858		20040318
US 2005208505	A1	20050922	US 2004-803648		20040318
US 2004241727	A1	20041202	US 2004-812731		20040330
PRIORITY APPLN. INFO.:			US 1999-115125P	P	19990106
			US 2000-477148	B1	20000104
			US 2002-268730	A2	20021009
			US 2003-601518	A2	20030620
			US 2004-802875	A2	20040312
			US 2004-812731	A	20040330

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:248643 CAPLUS
DOCUMENT NUMBER: 142:274056
TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 47
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004241727	A1	20041202	US 2004-812731		20040330
US 2004014059	A1	20040122	US 2002-268730		20021009
US 2005191637	A1	20050901	US 2004-803737		20040318
US 2005196762	A1	20050908	US 2004-803759		20040318
US 2005196763	A1	20050908	US 2004-803857		20040318
US 2005196764	A1	20050908	US 2004-803858		20040318
US 2005208505	A1	20050922	US 2004-803648		20040318
US 2004241727	A1	20041202	US 2004-812731		20040330
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			US 2000-477148	B1	20000104
			US 2002-268730	A2	20021009
			US 2003-601518	A2	20030620
			US 2004-802875	A2	20040312
			US 2004-812731	A	20040330

L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:60754 CAPLUS
Correction of: 2004:1036571
DOCUMENT NUMBER: 142:233342
Correction of: 142:16836
TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 29
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241727	A1	20041202	US 2004-812731	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2005191637	A1	20050901	US 2004-803737	20040318
US 2005196762	A1	20050908	US 2004-803759	20040318
US 2005196763	A1	20050908	US 2004-803857	20040318
US 2005196764	A1	20050908	US 2004-803858	20040318
US 2005208505	A1	20050922	US 2004-803648	20040318
US 2004265869	A1	20041230	US 2004-812716	20040330
US 2005208519	A1	20050922	US 2004-989191	20041115
PRIORITY APPLN. INFO.:			US 1999-115125P	P 19990106
			US 2000-477148	B1 20000104
			US 2002-268730	A2 20021009
			US 2003-601518	A2 20030620
			US 2004-802875	A2 20040312
			US 2004-812731	A2 20040330
			WO 2004-US20836	A2 20040621

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:977858 CAPLUS
DOCUMENT NUMBER: 138:52333
TITLE: Pharmaceutical composition for diagnosis, prevention or treatment of a tumorous state, comprising a modulator of the actin polymerization state
INVENTOR(S): Auclair, Christian; Amsellem, Valerie; Hervy, Martial; Subra, Frederic
PATENT ASSIGNEE(S): Bioalliance Pharma, Fr.; Ecole Normale Superieure De Cachan; Institut Gustave Roussy-IGR; Centre National de la Recherche Scientifique CNRS
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102846	A2	20021227	WO 2002-FR2106	20020618
WO 2002102846	A3	20040422		
WO 2002102846	B1	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2825928	A1	20021220	FR 2001-7976	20010618
FR 2825928	B1	20040402		
CA 2450845	AA	20021227	CA 2002-2450845	20020618
EP 1432732	A2	20040630	EP 2002-745538	20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005504521	T2	20050217	JP 2003-506318	20020618
US 2004191230	A1	20040930	US 2003-740266	20031218

PRIORITY APPLN. INFO.: FR 2001-7976 A 20010618
WO 2002-FR2106 W 20020618

=> d his

(FILE 'HOME' ENTERED AT 14:41:45 ON 17 APR 2006)

FILE 'REGISTRY' ENTERED AT 14:41:55 ON 17 APR 2006
E "DOLASTATIN"/CN 25
L1 1 S E6

FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006
L2 52669 S ACTIN
L3 812 S COFILIN
L4 1968300 S ANTAG? OR INHIBIT?
L5 222 S L4 (L) L3
L6 1659 S EWING?
L7 1 S L6 AND L5
L8 22 S L1
L9 0 S L8 AND L6
L10 224 S ZYXIN
L11 3 S L10 AND L6
L12 6 S L3 AND L6
L13 4 S L12 AND L4

=> s phosphoinositol?
L14 989 PHOSPHOINOSITOL?

=> s l14 and l6
L15 0 L14 AND L6

=> s phosphotidylinositol
96 PHOSPHOTIDYLINOSITOL
2 PHOSPHOTIDYLINOSITOLS
L16 98 PHOSPHOTIDYLINOSITOL
(PHOSPHOTIDYLINOSITOL OR PHOSPHOTIDYLINOSITOLS)

=> s l15 and l6
L17 0 L15 AND L6

=> file pctfull
COST IN U.S. DOLLARS SINCE FILE ENTRY 29.78 TOTAL SESSION 41.99

FULL ESTIMATED COST

FILE 'PCTFULL' ENTERED AT 14:49:15 ON 17 APR 2006
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FILE LAST UPDATED: 11 APR 2006 <20060411/UP>
MOST RECENT UPDATE WEEK: 200614 <200614/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
SEE
http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE
(last updated April 10, 2006) <<<

=> s cofilin
179 COFILIN
12 COFILINS

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L18         188 COFILIN
                (COFILIN OR COFILINS)

=> s ewing?
L19        3185 EWING?

=>

=> s l19 and l18
L20          19 L19 AND L18

=> s antag? or inhibit?
         53720 ANTAG?
        189862 INHIBIT?
L21     198141 ANTAG? OR INHIBIT?

=> s l20 and l21
L22          19 L20 AND L21

=> s l22 not py>2001
        488865 PY>2001
L23           4 L22 NOT PY>2001

=> d ibib 1-4

L23    ANSWER 1 OF 4     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2001055168 PCTFULL  ED 20020827
TITLE (ENGLISH):         NUCLEIC ACIDS, PROTEINS AND ANTIBODIES
TITLE (FRENCH):          ACIDES NUCLEIQUES, PROTEINES, ET ANTICORPS
INVENTOR(S):             ROSEN, Craig, A.;
                         BARASH, Steven, C.;
                         RUBEN, Steven, M.
PATENT ASSIGNEE(S):      HUMAN GENOME SCIENCES, INC.;
                         ROSEN, Craig, A.;
                         BARASH, Steven, C.;
                         RUBEN, Steven, M.
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 2001055168         A1 20010802

DESIGNATED STATES
       W:                AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
                         CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
                         IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
                         MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
                         TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
                         SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
                         DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
                         CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:       WO 2001-US1331        A  20010117
PRIORITY INFO.:          US 2000-60/179,065       20000131
                         US 2000-60/180,628       20000204
                         US 2000-60/184,664       20000224
                         US 2000-60/186,350       20000302
                         US 2000-60/189,874       20000316
                         US 2000-60/190,076       20000317
                         US 2000-60/198,123       20000418
                         US 2000-60/205,515       20000519
                         US 2000-60/209,467       20000607
                         US 2000-60/214,886       20000628
                         US 2000-60/215,135       20000630
                         US 2000-60/216,647       20000707
                         US 2000-60/216,880       20000707
                         US 2000-60/217,487       20000711
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US 2000-60/220,964	20000726
US 2000-60/225,757	20000814
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US 2000-60/225,758	20000814
US 2000-60/225,267	20000814
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US 2000-60/228,924	20000830
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US 2000-60/229,343	20000901
US 2000-60/229,287	20000901
US 2000-60/229,345	20000901
US 2000-60/229,513	20000905
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US 2000-60/230,438	20000906
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US 2000-60/231,413	20000908
US 2000-60/232,081	20000908
US 2000-60/231,244	20000908
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US 2000-60/236,370	20000929
US 2000-60/236,327	20000929
US 2000-60/237,039	20001002
US 2000-60/237,038	20001002
US 2000-60/237,040	20001002
US 2000-60/237,037	20001002
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US 2000-60/239,937	20001013
US 2000-60/239,935	20001013

US 2000-60/241,221	20001020
US 2000-60/241,808	20001020
US 2000-60/241,787	20001020
US 2000-60/240,960	20001020
US 2000-60/241,809	20001020
US 2000-60/241,785	20001020
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US 2000-60/246,523	20001108
US 2000-60/246,524	20001108
US 2000-60/249,299	20001117
US 2000-60/249,297	20001117
US 2000-60/249,244	20001117
US 2000-60/249,245	20001117
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US 2000-60/249,212	20001117
US 2000-60/249,213	20001117
US 2000-60/249,208	20001117
US 2000-60/249,218	20001117
US 2000-60/249,215	20001117
US 2000-60/249,211	20001117
US 2000-60/249,217	20001117
US 2000-60/249,216	20001117
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US 2000-60/249,264	20001117
US 2000-60/249,265	20001117
US 2000-60/249,300	20001117
US 2000-60/249,209	20001117
US 2000-60/250,160	20001201
US 2000-60/250,391	20001201
US 2000-60/256,719	20001205
US 2000-60/251,030	20001205
US 2000-60/251,988	20001205
US 2000-60/251,479	20001206
US 2000-60/251,869	20001208
US 2000-60/251,856	20001208
US 2000-60/251,868	20001208
US 2000-60/251,990	20001208
US 2000-60/251,989	20001208
US 2000-60/254,097	20001211
US 2001-60/259,678	20010105

L23 ANSWER 2 OF 4	PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:	1999051766 PCTFULL ED 20020515
TITLE (ENGLISH):	METHODS FOR PRODUCING LIBRARIES OF EXPRESSIBLE GENE SEQUENCES
TITLE (FRENCH):	METHODES DE PRODUCTION DE BANQUES DE SEQUENCES DE GENES EXPRIMABLES
INVENTOR(S):	FERNANDEZ, Joseph, Manuel;

HEYMAN, John, Alastair;
HOEFFLER, James, Paul;
MARKS-HULL, Heather, Lynn;
SINDICI, Michelle, Lynn

PATENT ASSIGNEE(S): INVITROGEN;
FERNANDEZ, Joseph, Manuel;
HEYMAN, John, Alastair;
HOEFFLER, James, Paul;
MARKS-HULL, Heather, Lynn;
SINDICI, Michelle, Lynn

LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9951766	A1	19991014

DESIGNATED STATES
W: AU CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.: WO 1999-US7270 A 19990402
PRIORITY INFO.: US 1998-09/054,936 19980403

L23 ANSWER 3 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999051620 PCTFULL ED 20020515
TITLE (ENGLISH): LIBRARIES OF EXPRESSIBLE GENE SEQUENCES
TITLE (FRENCH): BANQUES DE SEQUENCES DE GENES POUVANT ETRE EXPRIMEES
INVENTOR(S): FERNANDEZ, Joseph, Manuel;
HEYMAN, John, Alastair;
HOEFFLER, James, Paul

PATENT ASSIGNEE(S): INVITROGEN
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9951620	A1	19991014

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.: WO 1999-US7334 A 19990402
PRIORITY INFO.: US 1998-60/080,626 19980403
US 1998-60/096,981 19980818

L23 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1998041648 PCTFULL ED 20020514
TITLE (ENGLISH): TARGET GENES FOR ALLELE-SPECIFIC DRUGS
TITLE (FRENCH): GENES CIBLES POUR MEDICAMENTS SPECIFIQUES D'ALLELES
INVENTOR(S): HOUSMAN, David;
LEDLEY, Fred, D.;
STANTON, Vincent, P., Jr.

PATENT ASSIGNEE(S): VARIAGENICS, INC.;
HOUSMAN, David;
LEDLEY, Fred, D.;
STANTON, Vincent, P., Jr.

LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9841648	A2	19980924

DESIGNATED STATES
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW AT BE CH DE

DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-US5419 A 19980319
PRIORITY INFO.: US 1997-60/041,057 19970320

=> d kwic 2

L23 ANSWER 2 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . U3 52.36 60
snoRNP associated 55 kDa
protein
GI H-DO0096 Transtyretin (prealbumin) 16.28 20
C4 H-DO0408 Cytochrome P450 IIIA7 (P450- 55.44 64
HFLa)
M302 E7 H-DO0682 cofilin 18.37 30
M383 G2 H-DO0726 ferrochelatase 46.64 50.OkDa
M383 C3 H-DO0760 proteasome, subunit HO 25.85 34.OkDa
M305 B4 H-DO0761 proteasome, subunit HC5 26.62. . .
. . .
enoyl-Coenzyme A hydratase, 32.01 58
short chain, mitochondrial
El H-DI4446 Human HFREP- I mRNA for 34.43 40
unknown protein, complete cds
167-14 H-DI4497 H.sapiens (Ewing's sarcoma cell 51.44 64
line) mRNA encoding open
reading frame
M266 D2 H-DI4520 basic transcription element- 24.2 33.OkDa
binding protein 2
M318 D2 H-DI4658 hypothetical. . .
. . .
42.79 48
M298 C2 H-JO2611 apolipoprotein D 20.9 3 I.OkDa
M266 C4 H-JO2683 ADP/ATP carrier protein 32.89 36
M383 H2 H-JO2685 plasminogen activator inhibitor, 45.76
50.OkDa
placenta
167-3 H-JO2853 casein kinase 11, alpha chain 43.08 50
E3 H-JO2854 Human 20-kDa myosin light 19.03 31
chain (MLC-2) mRNA, complete
cds
M248. . .
. . .
transaldolase 37.18 39.OkDa
M423 C4 H-LI9593 Interleukin 8 receptor, beta 39.71 4 1.0kDa
G I H-LI9686 Homo sapiens macrophage 12.76 1 3
migration inhibitory factor (MIF)
gene, complete cds
G2 H-LI9739 metallopanstimulin 1 9.35 32
M302 E3 H-LI9871 activating transcription factor 3 20.02 36.OkDa
167-86 H-L20422 14 3 protein eta 34 1 3
M440 B2 H-L20492 Human garmna-glutamyl 24.86 35.OkDa
transpeptidase mRNA, complete
cds
M315 BI H-L20688 GDP-dissociation inhibitor 22.22 32
protein rhoA
M271 H3 H-L20941 ferritin, heavy polypeptide. 20.24 32
FERRITIN IS AN
INTRACELLULAR,
MOLECULE THAT STORES
IRON IN A SOLUBLE,
NONTOXIC, READILY
AVAILABLE FORM.
. . .
30

transforming protein rhoC,
Aplysia ras-related hornolog 9
M236 E3 H-L25085 Sec6l complex, beta subunit, 10.67 19
PROTEIN TRANSLOCATION
TN THE ENDOPLASMIC
RETICULUM
167-85 H-1,25610 cyclin-dependent kinase inhibitor 32
B2 H-L25610 cyclin-dependent kinase inhibitor 18.110 40
1
M297 H2 H-1,26232 cathepsin A/phospholipid transfer 54.34 64.OkDa
protein
167-4 H-1,26318 stress-activated protein kinase 52 42.31
JNKI
M428 Fl H-1,27586 Human TR4 orphan. . .
. . .
E2 H-MI9713 tropomyosin, alpha, muscle 31.35 4I.OkDa
167-79 H-MI9722 proto-oncogene tyrosine-protein 64 58.26
kinase FGR
M248 HI H-M20560 Annexin III (lipocortin III), 35.64 37
INHIBITOR OF
PHOSPHOLIPASE A2
M235 HI H-M20681 GLUCOSE TRANSPORTER 54.67 50
TYPE 3, BRAIN
167-29 H-M21616 beta platelet-derived growth 121 121.7
factor receptor precursor
M305 A3 H-M21812. . .
. . .
palmitoylated membrane protein, 51.37 5 I.OkDa
erythrocyte, 55 kDa
M302 C7 H-M65292 complement factor H-related 36.41 50
protein (GB:M65292)
D3 H-M68516 Human protein C inhibitor gene, 44.77 54
complete cds
167-27 H-M68520 cell division protein kinase 2 38 32.85
M236 D5 H-M68867 Cellular retinoic acid-binding 15.29 19.OkDa
protein 2,. . .
. . .
Al H-PO 197 S-adenosyhnethionine synthetase 42.46
2 (metX)
M365 BI H-PO203 hypothetical protein 10.12
M365 Cl H-PO209 hypothetical protein 49.61
M365 DI H-PO213 glucose inhibited division protein 68.42
(gidA)
M381 El H-PO218 hypothetical protein 20.24
M365 El H-PO221 nifLJ-Iike protein 35.97
M365 Fl H-PO227 outer m mbrane protein (omp5). . . C2 P]3 -]]
ribosomal protein SI (rps 1)
M366 D2 H-PO403 phenylalanyl-tRNA synthetase, 36.19
alpha subunit (pheS)
M366 E2 H-PO404 protein kinase C inhibitor 11.55
(SP:PI6436)
M366 F2 H-PO405 nifS-like protein 48.51
M366 G2 H-PO406 hypothetical protein 21.67
M366 H2 H-PO407 biotin sulfoxide reductase (bisC) 87.67
M381 DI H-PO409. . .
. . .
alanine racemase, biosynthetic 41.58
(a
M371 D6 H-PO942 D-alanine glycine perinease 49.61
(dagA)
M371 E6 H-PO943 D-arnino acid dehydrogenase 45.21
(dadA)
M371 F6 H-PO944 translation initiation inhibitor, 13.86
putative
M371 G6 H-PO946 conserved hypothetical integral 54.67

membrane protein
M371 H6 H-PO947 hypothetical protein 13.31
M371 A7 H-PO949 conserved hypothetical secreted 16.61
protein
M371 B7. . .
. . .
factor Ile, 48.360
alpha subunit
M302 D7 H-S69022 myosin, light polypeptide 2, 18.26 3 1
ventricular
H5 H-S69272 cytoplasmic antiproteinase=38 41.47 50
kda intracellular serine proteinase
inhibitor [human, placenta,
mRNA, 1465 nt]
DI H-S72043 GIF=growth inhibitory factor 7.59 19
[human, brain, Genornic, 2015 nt]
M266 B3 H-S74221 cytokine 1K factor 17.93 36.OkDa
DI H-S74445 cellular retinoic acid-binding 15.18 23
protein. . . small nuclear ribonucleoprotein, 13.97 17.OkDa
Sm D3
M311 D4 H-UI6660 enoyl-Coenzyme A hydratase-like 36.19 38
protein, peroxisomal
M302 H4 H-UI7074 cyclin-dependent kinase 6 18.59 29
inhibitor p 1 8
M306 A2 H-UI7195 A-kinase anchor protein I 00 72.05 100
[AKAPIOO*]
DI -UI7280 Steroidogenic acute regulatory 31.46 35
protein
M316 171 H-UI8291. . .
. . .
29.15 38.OkDa
factor TAF1132 mRNA, complete
cds
M424 H3 H-U22662 Human nuclear orphan receptor 49.28 49.OkDa
LXR-alpha mRNA, complete cds
M271 D2 H-U24074 killer cell inhibitory receptor 37.62 43
[KIR], Homo sapiens natural
killer-associated transcript 3
(NKAT3), complete cds.
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30
gamma
M416 D3 H-U26403 Human receptor tyrosine kinase 25.19 30.OkDa
ligand LERK-7 precursor
(EPLG7) mRNA, complete cds
M317 E2 H-U27143 human protein kinase C inhibitor- 13.900
17.OkDa
I cDNA
E5 H-U28249 Human II kd protein mRNA, 12.32 12
complete cds
F4 H-U28386 Human nuclear localization 58.3 54
sequence receptor hSRP. . . phosphatase 2A, 56.65 55.OkDa
regulatory subunit B' alpha- I
El H-U37529 Human substance P beta-PPT-A 14.3 22
mRNA, complete cds
M305 H5 H-U37547 apoptosis inhibitor 68.09 64
M424 D5 H-U38480 Human retinoid X receptor- 51.04 61.OkDa
gamma mRNA, complete cds
M270 F4 H-U38810 Human mab-21 cell fate-
determining protein. . . mRNA
M298 E4 H-U39945 human adenylate kinase 2 (adk2) 26.3633 38.OkDa
mRNA
166-38 H-U40282 human integrin-finked kinase 55 49.68
(ILK) mRNA
169-65 H-U40343 human CDK inhibitor p I 9INK4d 1 8 18. 33

mRNA
E2 H-U40705 Homo sapiens telomeric repeat 48.4 52
binding factor (TRF I) mRNA,
complete cds
166-50 H-U40989. . . E2 H-U47677 Human transcription factor E2F 1
48.18 53.OkDa
(E2FI) gene, promoter and
m421 H I H-U48707 Human protein phosphatase- 1 18.92 36.OkDa
inhibitor mRNA, complete cds
M302 B7 H-U49070 peptidyl-prolyl isomerase PIN I 18.04 28.OkDa
C1 H-U49188 Human placenta (Diff33) mRNA, 54.45 70
complete cds
M485 H2. . .
. . .
46.97 60.OkDa
phosphodiesterase (PDE4Q
mRNA, 4C-426 isoform,
complete cds
M306 F3 H-U66867 ubiquitin-conjugating enzyme E21 17.49 28
[UBE2I]
M416 E2 H-U681 11 Human protein phosphatase 22.66 37.OkDa
inhibitor 2 (PPP I R2) gene
F2 H-U68382 Mannosidase, alpha B, lysosomal 35.64 36
G2 H-U69141 Glutaryl-Coenzyme A 48.29 56
dehydrogenase
B2 H-U70660 Human copper. . . (HAHI) mRNA, complete
cds
M297 B2 H-U71374 peroxisomal membrane protein 40.15 40.OkDa
(Pexl3p)
M306 A3 H-U75272 progastricsin [PGC] 42.79 49.OkDa
A2 H-U75285 Homo sapiens apoptosis inhibitor 15.73 25
survivin gene, complete cds
B2 H-U77456 Human nucleosome assembly 41.36 50
protein 2 mRNA, complete cds
C2 H-U78294 Homo sapiens 15S-lipoxygenase 74.47. . . and VIIIa)
M302 B3 H-XO2751 proto-oncogene N-ras 20.9 25.OkDa
D3 H-XO2812 Human mRNA for transforming 43.12 50
growth factor-beta (TGF-beta)
M302 CI H-XO3124 tissue inhibitor of 22.88 T6.OkDa
metalloproteinase I
M362 BI H-XO3342 ribosornal protein L32 14.96 24.OkDa
M235 A2 H-XO3484 human mRNA for raf oncogene 71.350 73.OkDa
M318. . .
. . .
basic protein, 23 kDa 22.44 30.OkDa
M318 GI H-X57025 insulin-like growth factor 1 16.94 1 8
M305 F5 H-X57348 protein kinase C inhibitor 27.39 35.OkDa
M236 D6 H-X57351 interferon-induced protein 1-813 14.63 24
H3 H-X57352 interferon-induced protein 1-8U 14.74 38
M305 B6 H-X58079 S- I 00. . . 49
E2 H-X59357 Epstein-Barr virus small RNA- 14.19 36
associated protein
M236 D4 H-X59417 macropain, iota subunit, THE 27.17 36
INTERACTION OF CALPONIN
WITH ACTIN INHIBITS
ACTOMYOSIN MG-ATPASE
ACTIVITY
M271 H4 H-X59618 ribonucleotide reductase, small 42.9 46
subunit
M250 G3 H-X59710 CAAT-box DNA-binding protein, 22.66 34
subunit B, CCAAT-BINDING
TRANSCRIPTION FACTOR
SUBUNIT A [Homo. . .
. . .
H+ transporting, 42.13 58.OkDa

subunit C, vacuolar
M236 C3 H-X69392 ribosomal protein L26 16.06 29
B3 H-X69532 H.sapiens gene for inter-alpha- 100.32 98
trypsin inhibitor heavy chain HI,
exons 1-3
M236 F5 H-X69654 ribosomal protein S26 12.76 18
M421 C8 H-X70218 Protein phosphatase 4 (formerly 33.88
X), catalytic subunit
M266. . .

M235 BI H-X72841 Human retinoblastoma-binding 46.86 52.OkDa
protein (RbAp46) mRNA,
complete cds, IEF 7442
(GB:X72841)
217-25 H-X73428 DNA-binding protein inhibitor 20 17.08
ID-3
M305 B5 H-X73459 signal recognition particle, 15.07 20
subunit 14
M250 D6 H-X73460 ribosomal protein L3, isoform 2, 44.44 50.OkDa
COMPONENT OF. . .
. . .
H-YO0291 Human hap mRNA encoding a 49.39 59.OkDa
DNA-binding hormone receptor
M386 HI H-YO0345 polyadenylate-binding protein 69.74 70.OkDa
M469 A2 H-YO0630 Plasminogen activator inhibitor, 45.76
46.OkDa
type II (arginine-serpin)
M305 El H-YO0711 lactate dehydrogenase B 36.85 38.OkDa
H2 H-YO0764 ubiquinol/cytochrome c reductase 10.12 33
hinge protein
F5 H-YO7848 H.sapiens. . .

=> d kwic 4

L23 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ABEN . . .
loss of one of these alleles in cancer cells due to loss of
heterozygosity (LOH) and (2) the
development of inhibitors with high specificity for the single
remaining alternative allele of the
essential gene retained by the tumor cell after LOH.. . .
ABFR . . . perte de l'un de ces alleles dans des cellules cancereuses, due a
la perte
d'heterozygotie (LOH); et (2) developper des inhibiteurs
presentant une specificite elevee pour
l'allele distinct restant du gene essentiel retenu par la cellule
tumorale apres LOH. Des categories. . .

DETD Specifically, this invention is concerned with target genes for drugs
that are useful
for treating such diseases by providing allele-specific
inhibition of essential cell
functions.
. . .
strategy for the development of anticancer agents having a high
therapeutic
232/116
index is described in Housman, International Application PCT/US/94 08473
and
Housman, INHIBITORS OF ALTERNATIVE ALLELES OF GENES
ENCODING PROTEINS VITAL FOR CELL VIABILITY OR CELL GROWTH
AS A BASIS FOR CANCER THERAPEUTIC AGENTS, U.S.. . . which undergo
loss of
heterozygosity in a cancer. Treatment of a cancer in an individual who

is
heterozygous with an allele specific inhibitor targeted to the single allele of an
essential gene which is present in a cancer will inhibit the growth of the cancer
cells. In contrast, the alternative allele present in non-cancerous cells (which have
not undergone loss of heterozygosity). . . .
(3) identification of the absence of one of these alleles in cancer cells due to LOH and (4) development of specific inhibitors of the single
remaining allele of the essential gene retained by the cancer cell, but not the
alternative allele.

SUMMARY OF THE DWENTION
The utilization of inhibitors of alternative alleles, such as in the strategy described
in Housman, supra, requires the provision of suitable target genes in order to
identify such inhibitors and to implement corresponding diagnostic or therapeutic
methods. Thus, as described below, the present invention identifies useful groups
of genes which provide. . .

In each disease, the administration of such an inhibitor would have cytotoxic or
antiproliferative effects on the abnormally proliferating cells that exhibited LOH
and contained only the sensitive allele of the. . .

In addition, it was found that specific inhibitors of alternative alleles of an
essential gene would be useful in managing transplantation in instances where the
alleles in a donor bone marrow differ from the alleles in the recipient. For
example, administration of an inhibitor of an allele that was present in a donor
bone marrow but not the recipient could be used to treat graft-versus-host. . .

Alternatively, an inhibitor of an allele that is present in the recipient but not the
donor bone marrow could be used to enhance engraftment by preferentially creating space in the recipient bone marrow for the graft without inhibiting
proliferation of the engrafted donor marrow.

232/116
The term target gene refers to a gene where the gene, its RNA transcript, or its
protein product are specifically inhibited or potentially inhibited by a drug. In
references herein to genes or alleles, the term encoding refers to the entire gene
sequence, including both coding. . .
of alternative variances at a single variant site, or a combination of several different variances at different sites. In this invention, inhibitors targeted
to a specific allelic form or subset of the allelic forms of a gene can be targeted to

a specific variance. . .

. . .

dysplastic epithelium of
lung, breast, cervix, or other tissues. Drugs used in treating cancer and other
non-cancer proliferative disorders commonly aim to inhibit the proliferation of
cells and are commonly referred to as antiproliferative agents.

. . .

particular sequence
variance. Also preferably, these terms refer to loss of heterozygosity of a
particular sequence variance that is recognized by an inhibitor that will inhibit one
allele of the gene present in normal cells of the individual, but not an alternative
allele.

. . .

the individual clones. The alleles subject to LOH may vary from one
clone to another. Therefore treatment of these conditions preferably utilizes
inhibitors of at least two allelic forms. Thus, methods relating to such disorders
can utilize alternative alleles of one gene and/or allelic. . .

. . .

of LOH in certain locations, for example segments of
chromosomes 7,8,10,11,13,16, and 18 in prostate cancer, administration of an
allele-specific drug that inhibits one allele that is within such a region, in a patient
who is heterozygous for alternative forms of the gene, would. . .

. . .

genes, and provides, as examples, specific genes within those categories
which are found to be suitable as targets for allele specific inhibitors, in particular
for killing cancer cells or reducing the proliferation of cells in cancer or noncancer
proliferative disorders. Thus, the present invention. . . more variant
positions, indicates that the gene is a useful potential target gene in this invention
for the identification of allele specific inhibitors and in other aspects of the
invention.

. . .

those skilled in the art) identifying the gene and providing a known
sequence) which can be used for identifying allele specific inhibitors and for use in
other aspects of this invention. Preferably the gene has the LOH frequency and at
least one sequence variance. . .

. . .

vital for cell viability or growth, or essential
for cell survival and proliferation have the same meaning. A gene is essential if
inhibition of the function of such a gene or gene product will kill the cell or inhibit
its growth as determined by methods known in the art. Growth inhibition can be
monitored as a reduction or preferably a cessation of cell proliferation.

. . .

the affected gene, genetic disruption of the gene by homologous recombination
or other methods in organisms ranging from yeast to mice,

inhibition of the gene
by antisense oligonucleotides or ribozymes, and identification of the target of
known cytotoxic, drugs and other inhibitors. As further discussed below, the
essentiality of a gene can depend on the conditions to which the cell is exposed.

. . .
entity is absent or present at low levels, the
gene product is essential. In another example, the administration of a drug that
inhibits one or more functions within the cell can cause other functions to be
essential that are not essential in the absence. . .

. . .
Identification of one or more sequence variances in
that gene and/or in the corresponding gene products allows screening or design of
such inhibitors for potential treatment.

. . .
sequence variance, and therefore of individuals heterozygous for such
variances, indicates that the gene can be used for the identification of inhibitors
targeting allelic forms of the gene which have a particular variance or variances
and in the other aspects of this invention.

. . .
gene is a potential target. The
target gene, its RNA transcript or protein product can then be used as targets for
allele-specific inhibitors for treating the proliferative disorder or other uses as
described in the aspects of this invention.

. . .
of the
population are heterozygous for that gene provides genes which are particularly
likely to be useful target genes for allele specific inhibition in this invention.

. . .
or 50% of cases of such a disorder
indicates that the gene is useful as a potential target for identifying allele specific
inhibitors for the treatment of proliferative disorders and in other aspects of this
232/116
invention.

. . .
more preferably at least 30%, and most
preferably at least 40% are heterozygous in a specific population that may be
treated with inhibitors to treat cancer or other proliferative disorder in that
population. Once a specific variance is identified in a certain gene, the. . .

In the context of this invention, an alternative allele, or other reference to an
appropriate target for the inhibitors of this invention refers to a form of a gene
which differs in base sequence from at least,one other allele or. . . no
phenotypic effect on the physical condition of an individual having that variance
until the variance is targeted by an allele specific inhibitor

In connection with allele specific inhibitors and the methods of this invention, the terms allelic form or alternative form of the target gene or sequence variance within the. . . either or both of the gene or a product of that gene including the RNA transcript or protein product. Thus, a particular inhibitor may act in an allele specific manner (which will often be variance specific) at any of those levels and preferably the inhibitor is targeted to a particular sequence variance of the specific allelic form.

. . .

the classes described above in genes that are essential for cell survival or proliferation that can be the targets for allele-specific inhibitors for the treatment of cancer or noncancer proliferative disorders.

This invention provides inhibitors which are specific for at least one, but not all, allelic forms of a gene that encodes a gene product essential to cell growth or cell viability, for genes belonging to the specified categories of genes. The inhibitor may be active on the gene or gene product including the RNA transcript, protein product, or modifications thereof. Exposure to the inhibitor inhibits proliferation or kills cells which have undergone LOH of genes that are not inhibited by the drug and contain only an allelic form of the essential gene, its RNA transcript, or its protein product against which the inhibitor is targeted. Normal cells which contain two alternative alleles of the target genes, one of which is not inhibited by the specific inhibitor, are spared from the toxic effects of the inhibitor because the remaining activity of the allele which is not inhibited by the inhibitor is adequate to permit continued cell viability and growth. This differential effect of the inhibitor on cells with LOH of a targeted gene (e.g., a cancer cell) and normal cells accounts for the high therapeutic index of the inhibitors of this invention for the treatment of cancer or non-cancerous, proliferative disorders characterized by LOH. Toxicity of the inhibitor to normal cells is therefore low, compared to most currently available anticancer and antiproliferative agents.

. . .

indicated above and described in the Detailed Description of the Preferred Embodiments, in a first aspect the invention provides methods for identifying inhibitors potentially useful for treatment of a proliferative disorder, e.g., cancer. Such inhibitors are active on 232/116 specific allelic forms of target genes as identified herein. The method involves determining at least two allelic forms of such a gene encoding an

essential gene
product, and testing a potential allele specific inhibitor to determine whether the
potential inhibitor is active on, e.g., inhibits
expression of, at least one of the
allelic forms, but not all of those forms. If the potential inhibitor inhibits only a
subset of the allefic forms of the particular essential gene, then it is an allele
specific inhibitor. Preferably the difference in activity of the inhibitor for
different allelic forms is between allelic forms which have a sequence variance at a
particular site.

In many, or even most, cases an allele specific inhibitor discriminates between two
allelic forms due to a particular single sequence variance between the allelic forms
of the target gene. For example,. . . not affect the cleavage. In the Detailed Description of the
Invention specific examples of proteins, small molecules, and oligonucleotides
providing allele specific inhibition based on single sequence variances are
described. Thus, in preferred embodiments an allele specific inhibitor
discriminates between two allelic forms by discriminating a single sequence
variance. As previously indicated, inhibitors can be targeted to either the nucleic
acid or a polypeptide (where a nucleotide change results in an amino acid change).

In particular embodiments, the allele specific inhibitor will recognize more than
one linked sequence variances within a specific allele.

An allele specific inhibitor or variance specific inhibitor is a drug or inhibitor
that inhibits the activity of one alternative allele of a gene to a greater degree than
at least one other alternative allele. The difference in activity is commonly
determined by the dose or level of a drug required to achieve a quantitative degree
232/116
of inhibition. A commonly used measure of activity is the IC50 or concentration
of the drug required to achieve a 50% reduction in the measured activity of the
target gene. Preferably an allele specific inhibitor will have at least twice the
activity on the target allelic form than on a non-target allelic form, more
preferably at least. . . most preferably at least 100 times. This can also
be expressed as the sensitivities of the different allelic forms to the inhibitor.
. .
it is equivalent to state that the target allelic form is most preferably at least 100 times as sensitive to the inhibitor as a non-target allelic
form. The activity of an inhibitor can be measured either in vitro or in vivo, in

assay systems that reconstitute the in vivo system, or in systems incorporating
selected elements of the complete biological system. For use in inhibiting cells
containing only the target allelic form rather than cells containing at least one non-
targeted allelic form, the difference in activity. . .

In a related aspect, the invention provides inhibitors potentially useful for tumor,
e.g. . cancer treatment, or treatment of other proliferative disorders. Such
inhibitors are active on a specific allele of a gene which has at least two different
alleles encoding an essential gene product in one of the target gene categories
above. Such inhibitors can, for example, be identified by the above screemng
methods.

In a related aspect, the invention provides methods for producing inhibitors active
on such specific allelic forms of belonging to one of the above categories genes by
232/116
identifying a gene encoding an essential. . . product which has alternative allelic
forms in a non-tumor cell and which undergoes LOH in a tumor cell, screening to
identify an inhibitor which is active on at least one but less than all of the alleles
of the gene, and synthesizing the inhibitor in an amount sufficient to produce a
therapeutic effect when administered to a patient suffering from a tumor in which
tumor cells have only the allele on which the inhibitor is active.

In the context of this invention, the term active on an allefic form or allele
specific inhibitor or specific for an allelic form indicates that the relevant
inhibitor inhibits an allele having a particular sequence to a greater extent
(preferably > 2x) than an allele having a sequence which differs in a particular
manner. Thus, for alleles for which a particular base position is identified, the
inhibitor has a higher degree of inhibition when a certain base is in the specified
position then when at least one different base is in that position. This. . . means that
for substitution at a particular base position, at least two of the possible allelic
forms differ in sensitivity to an inhibitor. Usually, however, for a specific
sequence variance site, the site will be occupied by one of only two bases.

Further, if an inhibitor acts at the polypeptide level, and any of three bases may be
present at a particular position in a coding sequence but only one of the
substitutions results in an amino acid change, then the activity of the inhibitor

would be expected to be the same for the two forms producing the same amino
acid sequence but different for the form. . .

The term less active indicates that the inhibitor will inhibit growth of or kill a
cell containing only the allelic form of a gene on which the inhibitor is more active
at concentrations at which it does not significantly inhibit the growth of or kill a
cell containing only an allelic form on which the inhibitor is less active.

232/116
The term drug or inhibitor refers to a compound or molecule which, when
brought into contact with a gene, its RNA transcript, or its gene product which the
compound inhibits, reduces the rate of a cellular process, reduces the level of a
cellular constituent, or reduces the level of activity of. . . the term to those skilled in the art and not limiting. Thus, the term generally indicates that a compound has an inhibitory effect on a cell or process,
as understood by those skilled in the art. Examples of inhibitory effects are a
reduction in expression of a gene product, reduction in the rate of catalytic activity
of an enzyme, and reduction. . . formation or the amount of an essential
cellular component. The blocking or reduction need not be complete, in most
cases, for the inhibitor to have useful activity. Thus, in the present invention,
inhibitors are targeted to genes, their RNA transcript, or their protein product
that are essential for cell viability or proliferation. Such inhibitors would have the
effect of inhibiting essential functions, leading to loss of cell viability or inhibition
of cell proliferation. In preferred embodiments, such inhibitors cause cell death or
stop cell proliferation. In preferred embodiments of this invention, inhibitors
specifically include a molecule or compound capable of inhibiting one or more,
but not all, alleles of genes, their RNA transcript, or their protein product that are
essential for cell survival or proliferation. The terms inhibitor of a gene or
inhibitor of an allele as used herein include inhibitors acting on the level of the
gene, its gene product, its RNA transcript, its protein product, or modifications
thereof and is explicitly not limited to those inhibitors or drugs that work on the
gene sequence itself.

Several types of inhibitors are generally recognized in the art. A competitive
inhibitor is one that binds to the same site on the gene, its RNA transcript or gene
product as a natural substrate. . . is required for the action of the gene
or gene product, and competitively prevents the binding of that

substrate. An
232/116
66 allosteric inhibitor is one that binds to a gene or gene product and alters the
activity of the gene or gene product without preventing binding of a substrate or
cofactor. Inhibition can also involve reducing the amount of the gene, RNA
transcript, or its protein product, and thus the total amount of activity from the
gene in the cell. Such inhibition can occur by action at any of a large number of
different process points, including for example by inhibiting transcription or
translation, or by inducing the elimination of the gene, its RNA transcript, or its
protein product where elimination may involve. . . of the target or egress or export from the compartment in which it is active and the process of
excretion or export. Inhibition can also be achieved by modifying the structure of
the target, interfering with secondary modifications, or interfering with cofactors
or other ancillary components which are required for its activity. Inhibitors can be
comprised of small molecules or polymeric organic compounds including oligopeptides or oligonucleotides.

The term active on a gene or targeted to a gene indicates that an inhibitor
exerts its inhibitory effect in a manner which is preferentially linked with the
characteristic properties of a gene, its RNA transcript or its gene. . . RNA with other cellular constituents (RNA, protein, cofactors, substrates, etc.)
required for activity. Thus, in general these terms indicate that the inhibitor acts
on the gene, its RNA transcript, its protein product, its gene product, or
modifications thereof, or on a reaction or reaction. . .

. . .
from one of the
above categories has undergone loss of heterozygosity. The method involves
administering a therapeutic amount of an allele specific inhibitor of such an
essential gene to a patient whose normal somatic cells are heterozygous for that
gene but whose tumor cells contain only a single allelic form of the gene. The
inhibitor is active on the specific allele of the gene present in the tumor cells.

. . .
cancer. The method involves administering to a patient having a precancerous condition or an early stage cancer or cancers an allele specific
inhibitor targeted to an allele of an essential gene for which the normal somatic
cells of the patient are heterozygous and which. . . the precancerous condition are not clonal from a single cell, the method involves
subsequently administering to the patient a second allele specific inhibitor in an
amount sufficient to inhibit and preferably kill cells with LOH in which an allele

not targeted by the first inhibitor is the only remaining allele of the gene. In most cases, the second allele specific inhibitor will target the alternative allele of the gene targeted by the first inhibitor. However, the second inhibitor can also target an allele of a second essential gene which has undergone LOH. The second gene may have undergone LOH in. . . affected the first gene due to their proximity on a chromosome, though this is not essential. Additionally, in other cases, allele specific inhibition of one of the alleles of each of 3, 4, or even 232/116 more target genes can be utilized in a serial. . . genes need not be tightly linked so that LOH of the various genes does not necessarily occur together. By using the serial inhibition of an allele of each of the target genes, it is possible to inhibit and preferably kill the full population of precancerous cells in which LOH has occurred. Thus, the net effect is essentially the same as if allele specific inhibitors of each of the two alternative alleles of one essential gene had been used.

In the context of the administration of multiple allele specific inhibitors, the terms serial or subsequently indicates that the administration of two or more inhibitors is sufficiently temporally separated so that normal somatic cells remain functional and are therefore able to survive and/or proliferate. Those skilled. . . that the required time will depend on various factors, such as clearance rate, type and extent of the effect of an inhibitor on normal cells, and additive cellular toxicity, and that appropriate timing can be routinely determined for particular selections of compounds.

In another related aspect, the invention provides a method for identifying a potential patient for treatment with an inhibitor active on a specific allele of an essential gene from one of the above categories. The method involves identifying a patient having. . . the neoplastic cells contain only a single allele of the gene, then the patient is a potential patient for treatment with the inhibitor.

With respect to identifying patients with precancerous or oligoclonal proliferative 232/116 diseases characterized by LOH, and selecting appropriate allele or variance-specific inhibitors for such patients, in some cases it may not be practical to obtain samples of all proliferative lesions for LOH assays... . . aorta cannot routinely be sampled by biopsy, and dysplastic lesions in the cervix, colon, or bronchus can be multifocal. Therefore, allele specific inhibitors can be selected for such conditions based on previously established

patterns of LOH for the condition, and on specific testing for. . . . . most preferably 100%. However, it is not necessary that 100% of lesions show LOH for a successful treatment by allele specific inhibitors because 2,3,4, or even more inhibitors can be used in a combined approach to target an ever higher fraction of lesions, and because substantial therapeutic benefit may be achieved by inhibiting the proliferation of less than 100% of lesions.

In another aspect, the invention provides a method for identifying a potential patient undergoing transplantation for treatment with an inhibitor active on a specific allele of an essential gene from one of the above categories. The method involves identifying a patient undergoing. . . . . related aspect, the invention provides a method for treating graft versus host disease in allogenic transplantation in which an allele specific inhibitor is used to inhibit proliferation of donor cells, e.g. . to inhibit stimulation of the donor immune system. In preferred embodiments, the allele specific inhibitor is selected by identifying alternative variances or allelic forms of an essential gene that are present in the donor tissues but not the recipient. Therapy with a variance or allele specific inhibitor or inhibitors that recognizes both alleles of the essential gene that are present in the donor, but not both alleles of the same. . . . . another aspect, the invention provides a method for enhancing engraftment of an allogenic bone marrow transplant in which an allele specific inhibitor is used to kill or suppress the patient's own bone marrow, providing space for engraftment of the donor cells within the marrow cavity. In preferred embodiments, the allele specific inhibitor is selected by identifying alternative forms of an essential gene that are present in the recipient but not the donor marrow. Therapy with an allele specific (generally a variance specific) inhibitor that recognizes both forms of the essential gene that are present in the recipient, but not both forms of the same gene. . .

Allele specific inhibitors can be used to treat or prevent chimerism by selectively killing or suppressing proliferation of the patient's own cells without toxicity. . . . . aspect, the invention provides a method for treating cancer in a patient receiving allogenic or autologous transplantation in which an allele specific inhibitor is used to kill or inhibit the growth of cancer cells without toxicity to the transplanted marrow. In one embodiment, in an autologous, transplantation the

allele specific inhibitor is selected to recognize one alternative allele of an essential gene remaining in the cancer cell due to LOH in patients. . . therapy of cancer without suppression of the transplanted marrow. In an alternative embodiment, in an allogenic transplantation, therapy with an allele specific inhibitor that recognizes the one form of the essential gene that is present in cancer cells due to LOH in the recipient,. . . tissue for selective reimplantation. The present invention provides for an improved method for purging bone marrow of malignant cells using allele specific inhibitors of essential genes. The method involves identifying an essential gene with only one variant form remaining in the cancer cells due. . . The patient's bone marrow is then cultivated ex vivo using methods known in the art in the presence of an allele specific inhibitor that inhibits the allele that is present in the cancer cells, but not the alternative allele that is present in the heterozygous normal bone. . .

In another aspect, the invention provides a method for inhibiting growth of or killing a cell containing only one allelic form of a gene by contacting the cell with an inhibitor active on that allelic form. The gene has at least two sequence variants in a population, and belongs to one of the categories of essential genes described below. The inhibitor is less active on at least one other allelic form of the gene.

In preferred embodiments of the above aspects in which an allele specific inhibitor is used to inhibit a cell or to treat a patient, a plurality of different inhibitors may be used. Preferably different inhibitors target a plurality of different variances in a single target gene, or target variances in different target genes, or both. In particular embodiments a plurality of inhibitors is used simultaneously, in others there is serial administration using different inhibitors or different sets of inhibitors in separate administrations, which may be performed as a single set of administrations in which each set of inhibitors is administered once, or in multiple serial administrations in which each set of inhibitors is administered more than once. Such use of multiple inhibitors provides enhanced inhibition, which preferably includes killing, of the targeted cells. In addition, allele specific inhibitors as described can be used in conjunction with other treatments for diseases and conditions, including in conjunction with other chemotherapeutic agents such. . .

In a related aspect, an allele specific inhibitor can be used in conjunction with a conventional antiproliferative or chemotherapeutic agent or therapy, such therapies including radiation, immunotherapy, or surgery. In. . . . with the above aspects, in a further aspect the invention provides a pharmaceutical composition which includes at least one allele specific inhibitor.

In preferred embodiments the composition includes at least one allele specific inhibitor and a pharmaceutically acceptable carrier. Such carriers are known in the art and some commonly used carriers are described in the Detailed Description below. Also in preferred embodiments the composition includes two, three, or more allele specific inhibitors, and may also include a pharmaceutically acceptable carrier. In other preferred embodiments, the composition includes at least one allele specific inhibitor and another antineoplastic agent, which need not be an allele specific inhibitor. The embodiments of this aspect may also optionally include diluents and /or other components as are commonly used in pharmaceutical compositions or formulations. In embodiments having a plurality of allele specific inhibitors, the inhibitors may target a plurality of different variances of a single target essential gene, or may target sequence variances of a plurality of. . .

232/116
In accord with the use of pharmaceutical compositions, the present invention also provides a packaged pharmaceutical composition comprising an allele specific inhibitor as described above, bearing a Food and Drug Administration use indication for administration to a patient suffering from a cancer or. . .

Thus, similar to the above, the invention provides a method for identifying an inhibitor potentially useful for treatment of cancer or other proliferative disorder.

The inhibitor is active on a conditionally essential gene, and the gene is subject to loss of heterozygosity in a cancer. The method. . . least two alleles of a said gene which differ at at least one sequence variance site and testing a potential allele specific inhibitor to determine whether the potential inhibitor is active on at least one but less than all of the identified alleles. If the potential inhibitor inhibits expression of at least one but less than all of the alleles or reduces the level of activity of a product of at least one but less than all of the alleles, this indicates that the potential allele specific inhibitor is, in fact such an allele-specific

inhibitor inhibitor.

Similar to other types of target genes described above, the invention provides
inhibitors, methods for producing inhibitors,
pharmaceutical compositions, methods
for identifying potential patients, probes, and primers which target or recognize
alleles of a conditionally essential gene or utilize inhibitors
which target such genes.

. . .
also provides methods for preventing the development of cancer,
methods for treating a patient suffering from a cancer, and methods for inhibiting
growth of a cells as described above except that the targeted cells are subjected to an
altered condition such that the gene. . .

232/116
In still another aspect, not requiring the use of allele specific inhibitors, but still
utilizing information about sequence variance or allelic differences between normal
somatic cells and cancer cells in a patient, the invention. . .

. . .
above aspects, a conventional therapy acts on a protein
or other molecular target in the same pathway as the allele specific inhibitor. As an
example, the antineoplastic drug hydroxyurea, which inhibits ribonucleotide
reductase (RR), can be used in conjunction with an allele specific inhibitor of RR
subunit MI or M2 or another gene that encodes a product important in nucleotide
synthesis. Similarly, the antiproliferative drug methotrexate inhibits the enzyme
dihydrofolate reductase (DHFR), and can be used with allele specific inhibitors of
DHFR that would result in a differential methotrexate effect on cancer tissues
compared to normal proliferating tissues. Alternatively, methotrexate can be used
with allele specific inhibitors of other genes important in folate metabolism to
achieve an enhanced cancer cell specificity for methotrexate. Similarly, the
anticancer drug 5-fluorouracil and related compounds can be administered together
with an allele specific inhibitor of thymidylate synthase (TS) in a patient
heterozygous for TS and with LOH at the TS gene in proliferating cells, e.g., cancer
cells. Alternatively, an allele specific inhibitor of 5-FU degradation or metabolism
can be administered with 5-FU. For example, the enzyme dihydropyrimidine
dehydrogenase, which catalyzes the first and rate. . .

. . .
LOH in one or more tumors or other
proliferative disorders. Genes having these characteristics can then be used for
identifying allele specific inhibitors and evaluated for use in the other methods of
this invention. Such procedures are routine, as is shown by the Detailed
Description. . .

In preferred embodiments of the above methods and inhibitors involving particular target genes or classes or categories of genes, the inhibitor or potential inhibitor is a ribozyme which is designed to specifically cleave a particular target allelic form of a gene (i.e., a nucleotide sequence such. . .

Similarly, in preferred embodiments the inhibitor or potential inhibitor is an oligonucleotide, e.g, an antisense oligonucleotide, preferably at least partially an oligodeoxyribonucleotide. The antisense oligonucleotide is complementary to a sequence which includes. . .

Thus, derivatives of nucleic acid inhibitors include modified nucleic acid molecules which may contain one or more of: one or more nucleotide analogs, including modifications in the sugar. . .

Similarly, in preferred embodiments the inhibitor or potential inhibitor is an antibody, preferably a monoclonal antibody, which may be complexed or conjugated with one or more other components, or a fragment. . .

An inhibitor may also be an oligopeptide or oligopeptide derivative. Such peptides may be natural or synthetic amino acid sequences, and may have modifications. . .

In other embodiments, the inhibitor is a small molecule, for example, a molecule of one of the structural types used for conventional anticancer chemotherapy.

. . .

region undergoes LOH at frequencies similar to the marker. Such gene identification thus further identifies particular cancers which can potentially be treated with inhibitors targeting sequence variances in those essential genes.

. . .

LOH for other such disorders and cancers, and can further readily identify essential genes which are potential targets for variance specific inhibition and the treatment of the corresponding condition and in other aspects of this invention.

. . .

72 hours after transfection with antisense oligonucleotides. Anti-ras is an oligonucleotide known to have antiproliferative effects against T24 cells. This oligonucleotide exhibits inhibition comparable to the anti-RPA70 oligonucleotide.

. . .

is two graphs showing that the proliferation of two cell lines homozygous for different variant forms of the RPA70 gene is inhibited to a greater degree by matched oligonucleotides than by oligorners having a single base mismatch. Cell proliferation was measured by BrdU incorporation. . .

232/116
Fig. 13 is a graph showing Inhibition of BrdU incorporation in A549 cells by
antisense oligonucleotides against the RPA 70 gene. Cells were transfected, as
described previously, with a. . .

Fig. 20 is a graph showing inhibition of mutant ras using antisense
oligonucleotides specific for the mutant form, based on information available in
Schwab et al., 1994, PNAS 91:10460. . .

. . .
and
the variant sequences within these genes, have utility for the therapy of cancer and
other disorders through the discovery of variance-specific inhibitors.

Gene targets for a variance-specific inhibition strategy in this invention satisfy three
criteria.

A large number of references have identified essential genes which constitute actual
or potential targets for allele specific inhibition. The identification of essential genes
can be approached in various ways.

. . .
carbohydrates, lipids, organic ions, and inorganic ions, or cytoskeletal elements. The loss of homeostasis often results in cell death or apoptosis or
inhibition of cell proliferation. Homeostasis in a living cell is dynamic, and
programed changes in homeostasis are required through the life cycle. .
.

. . .
those genes whose products are required for maintaining this homeostasis conducive to cell growth and survival are targets for anti-neoplastic
e.g., anti-cancer, inhibitors as described in the methods herein. For example, many
genes are involved in synthetic functions, allowing the cells to produce essential
cellular. . .

. . .
affecting the gene in a neoplastic disorder, establishes that the gene is a target gene potentially useful for identifying allele specific inhibitors
and for other aspects of the invention. In addition, as described, target genes are
useftil in embodiments of certain aspects of the. . .

. . .
(Type I Beta) L25441
GGTI3 (Geranylgeranyltransferase) Y08201
Geranylgeranyltransferase (Type 11 Beta-Subunit) X98001
3.5 Genes required for regulation of levels of organic ions
Gdp Dissociation Inhibitors
GDI Alpha (RAB GDP Dissociation Inhibitor Alpha) D45021
Rab Gdp (RAB GDP Dissociation Inhibitor Alpha) D13988
4) Genes Required to Maintain Cellular Proteins at Levels Compatible with Cell Growth or Survival
Polypeptide precursor biosynthesis
Amino acid biosynthesis and. . . processing peptidase alpha subunit)

D50913
MMP7 X07819
Proteasorne Beta 6 D29012
Proteasome Beta 7 D38048
Proteasorne C13 U 1 7496
232/116
Proteasome C2 D00759
Proteasome C7-1 D26599
Proteasome inhibitor hPI31 subunit D88378
Proteasome P I 12 D44466
Proteasome P27 ABOO3177
Proteasome P55 ABOO3103
Ubiquitin System
Enzyme E2-17 Kd(Cyclin-selective ubiquitin carrier protein) U73379
ISOT-3(Ubiquitin carboxyl-terminal hydrolase. . .
. . .
Cell Shape and Motility at Levels
Compatible with Cell Growth or Survival
Cell structure genes (Cytoskeleton)
Actin X04098
Beta-Centractin X82207
Capping Protein Alpha U03851
CFL I (Cofilin, Non-Muscle Isoform) X95404
Desmin J03191
Dystrophin U26743
Gelsolin X04412
hOGG I (Myosin Light Chain Kinase) ABOO0410
IC Heavy Chain U31089
Itga2 (Integrin, Alpha 2 (CD49B, alpha. . .

Therapy with inhibitors of conditionally essential genes involves administration of the inhibitor together with a chemical or physical elements that causes the target gene to be essential for cell survival or proliferation. The use of allele specific inhibitors in the current invention allows specific killing of cancer cells with such chemical or physical agent since the gene function that is essential for the survival of cells (in the presence of the chemical or physical agent) is inhibited in the cancer cell but not in the normal cell.

. . .
are responsible for maintaining cell survival or proliferation in the presence of a drug or biological material. For example, a drug that inhibits one pathway for maintaining the level of a cellular constituent within levels required for cell survival or proliferation may make alternative pathways essential. In a specific embodiment, the inhibition of a synthetic pathway for a cellular constituent may make alternative synthetic pathways essential for cell survival or proliferation. Alternatively, a. . . from the cell essential for continued survival or proliferation. It will be evident to those skilled in the art that anything which inhibits the ability of a cell to survive in the presence of a specific drug that is designed to be cytostatic or cytotoxic, will sensitize that cell to the effects of the drug. A chemosensitizing agent is one that inhibits a function

in the cell that is
conditionally essential due to the administration of a chemotherapeutic drug.

. . .

in DNA repair may be essential that are not essential in the absence of the
external physical force. An agent that inhibits functions in the cell that are essential
due to the adminitration of ionizing radition would be termed a radiosensitizing
agent.

. . .

physical factors, determining whether
such genes are subject to loss of heterozygosity, identifying alternative alleles in
these genes and developing allele specific inhibitors of alternative forins of the gene.

The administration of such an inhibitor to a patient who has two alternative forms of
the gene in normal cells but only one in the cancer cell. . .

Thiopurinemethyltransferase (GenBankU12387)
e. Inactivation or transformation of other drugs including, but not limited to, purine analogs, folate analogs, topoisomerase inhibitors
and tubulin acting drugs via specific enzymatic modification.

I-kappa B alpha (GenBank M69043)
Increased expression of exogenous I kappa B-alpha, an inhibitor of
NF-kappa B, increases cell sensitivity to ionizing radiation. Thus is conditionally essential for cells exposed to ionizing radiation.

. . .

affect the gene sequence, RNA
sequence, or protein sequence of the gene or its gene products, which would
facilitate the design of inhibitors of the protein product, or be a base difference
anywhere within the genomic DNA sequence, including the promoter or intron
regions. Such DNA sequence variance can be exploited to design inhibitors of
transcription or translation which distinguish between two allefic forms of the
targeted gene. Sequence variants that do not alter protein sequence. .

. . .

genes located in regions which are
characteristically associated with LOH for a particular cancer, or other tumor are
particularly advantageous targets for inhibitors useful for treatment of that cancer or
tumor because such genes will also characteristically undergo LOH at high
frequency. The fact that. . . LOH occurs before the clonal expansion of cancers
in precancerous, abnormally proliferating tissue is potentially useful for preventing
cancer with allele specific inhibitors of essential genes.

. . .

disorder will indicate that the allele specific
treatment would be appropriate for the disorder. For the application of the general
allele specific inhibition strategy to such conditions (e.g..

selection of target gene
and variance, identification of inhibitors, selection of
composition and
administration method appropriate for the condition and the
inhibitor), the cells
associated with the condition correspond with the tumor, e.g., cancer
cells, for the
232/116
methods described in the Summary above.

. . .
at least one marker. This does not
necessarily represent the maximum fraction of plaques which could
potentially be
treated with allele specific inhibitors because the study did
not attempt to determine
the sites of maximum LOH on each arm. LOH which is partial arm. . .

. . .
allele of the essential
gene is lost from the patient's cancer cells, the retained allele can be
targeted with an
allele specific inhibitor. Such an inhibitor will
kill, or reduce or prevent the growth
of cancer cells by abolishing the fimction of an essential gene. Normal
cells, which
retain both uninhibited and inhibited alleles, will survive or
grow due to the
expression of the uninhibited allele. This is clearly indicated because
tumor cells
having only one allelic form (after LOH) thrive, thus, normal cells will
also
function normally with one of two allelic forms inhibited.

. . .
neuroectodermal
tumor
Rhabdomyosarcoma
17q Breast carcinoma
Neurofibroma: N171
22q Acoustic neurinoma
1 8 Renal cell carcinoma Colorectal carcinoma
18q Breast carcinoma Ependymoma
Colorectal carcinoma Meningioma
Neurofibroma
V. Use of variance-specific inhibitors of essential genes to
treat non-malignant,
proliferative conditions.

. . .
will differ, with, for example, allele A
of a hypothetical essential gene lost in some plaques and allele A' in
others. An inhibitor of allele A would be expected to kill (or
arrest
growth of) only about half of all the plaques with allele. . .
plaques hernizygous for A. To kill the other
half of the plaques with allele loss at the target locus would require
an
inhibitor of A'. Simultaneous use of inhibitors of A
and A' would be
highly toxic to diploid normal cells. However serial use of an
inhibitor
directed to allele A followed by an inhibitor directed to A'
(perhaps
repeating treatment for several cycles, or even indefinitely) would
alternately abolish essential gene function in one half of all haploid
plaque
cells and then the other half, leading eventually to death or sustained
inhibition of proliferation of all plaque cells. Normal cells

would retain
232/116
50% gene function in the presence of inhibitor (either from allele A or
allele A'). This therapeutic approach is applicable to the eradication of
any clonal proliferation of cells in. . .
. . .
surgically removed, LOH has been well described. As
with atherosclerotic plaques, these tumors are frequently multifocal and
therefore the approach of serial inhibition of allele A followed by
inhibition of allele A' would alternately abolish essential gene function in
one half of all haploid tumor cells and then the other half, leading
eventually to death or sustained inhibition of proliferation of all tumor
cells.
. . .
one allelic form in individuals whose normal somatic cells are
heterozygous for the particular essential gene. The essential gene can therefore
be inhibited by an allele specific inhibitor, i.e., a variance specific inhibitor. In
some conditions, however, multiple, independently arising lesions in an
individual are subjected to LOH in a disease or condition, e.g., in. .
.

It was determined that such conditions can be treated using allele specific
inhibitors despite the presence of both alleles in cells related to the condition.

There are two strategies for such therapy. The first is to serially administer
different inhibitors targeted to the different allelic forms of the target gene. This
can be accomplished by using inhibitors which target the alternative sequence
variants of one sequence variance site. Simultaneous administration of inhibitors
of both allefic forms of an essential gene would inhibit the cells which have
undergone LOH at that gene, but would also inhibit the normal heterozygous cells
of the individual. This treatment would inhibit essential ftinctions in normal cells
as well as cancer cells and have no advantage ~~over~~ the administration of
conventional antiproliferative drugs, many of which are inhibitors of known
essential functions. In contrast, administration of the first inhibitor targets the
subset of cells which have only the first allelic form of an essential gene. As
described for the general strategy, this inhibitor will not significantly affect the
growth or survival of the normal heterozygous somatic cells. This first
administration is followed by administration of a second inhibitor; the second
232/116
inhibitor targets the cells which contain only the second allelic form of the gene,
and again does not significantly affect the normal. . . will
be useful. Similarly, recurring, or even indefinitely continued alternating

administrations will provide useful treatment. Likewise, these methods can
incorporate the use of inhibitors targeted to specific alleles
of a plurality, e.g., 2,
3, 4, or more different target genes.

. . .

in non-malignant diseases are not
clonal, there may be systematic loss of one parental chromosome allowing
effective therapy with only one variance-specific inhibitor.
This would occur, for
example, if there were an inherited or early embryonic mutation within a tumor
suppressor gene on one parental. . . of the corresponding normal tumor suppressor
gene on the other parental chromosome would lead to abnormal
proliferation. In
such cases a variance-specific inhibitor of an essential gene
that was closely
linked to the normal tumor suppressor gene would preferentially kill cells in the
proliferating lesion.

VI. Characteristics of allele-specific inhibitors
As indicated above allele specific inhibitors or allele
specific anti-neoplastic
agents represent a new approach to tumor therapy because they are lethal or
significantly inhibit the growth only of tumor cells. The
advantages of this
approach include, first, lack of toxicity to the normal cells of. . .
a therapeutic index greater than that of conventional tumor, e.g., cancer
chemotherapy drugs, and second, it is not necessary that the
inhibitors be targeted
specifically to the tumor cells, as they can be administered
systemically. As also
described above, usually an allele specific inhibitor is
specific for a single
232/116
sequence variance of an essential gene, though in some cases the
inhibitor utilizes
the joint effects of two or more sequence variances on a particular allele.

It is not necessary for the allele specific inhibitor to have
absolute specificity.

. . .

of a gene product
encoded by the essential gene will often show a reduction in gene activity when
they take up the inhibitors of this invention, but should
remain viable due to the
activity of the protein encoded by the uninhibited allele. On the other hand,
tumor cells expressing only one allele due to LOH, will respond to the inhibitors
of this invention which are specifically directed to the remaining allele, with a
greater reduction in gene activity. Growth of tumor cells exposed to the
inhibitors of this invention will be inhibited due
to the suppression of either the
synthesis or the biological activity of the essential gene product.

. . .

only two allelic forms in any given individual, the
gene can have more than two allelic forms in a human population.

Accordingly, inhibitors can be targeted to any of the alleles in the population. A particular inhibitor will generally be targeted to a subset of the allelic forms; the members of the subset will have a particular sequence variance which provides the specific targeting. In some cases, however, the inhibitor will jointly target two, or possibly more sequence variances.

Once two or more alleles are identified for a target essential gene, inhibitors of high specificity for an allele can be designed or identified empirically. Inhibitors that can be used in the present invention will depend on whether allelic variation at a target locus affects the amino acid. . . the mRNA sequence, or the DNA in intron and promoter regions. If there is variation at the protein level, then classes of inhibitors would include low molecular weight drugs, oligopeptides and their derivatives, and antibodies, including modified or partial
232/116
antibody fragments or derivatives. For mRNA or DNA sequence variance the main class of inhibitors are complementary oligonucleotides and their derivatives and catalytic RNA molecules such as ribozymes, including modified ribozymes.

The generation of inhibitors of this invention can be accomplished by a number of methods. The preferred method for the generation of specific inhibitors of the targeted allelic gene product uses computer modeling of both the target protein and the specific inhibitor. Other methods include screening compound libraries or microorganism broths, empirical screening of libraries of peptides displayed on bacteriophage, and various immunological approaches.

Further, in the treatment of cancer patients, a therapeutic strategy includes using more than one inhibitor of this invention to inhibit more than one target. In this manner, inhibitors directed to different proteins essential to cell growth can be targeted and inhibited simultaneously. The advantage of this approach is to increase the specificity of the inhibition of proliferation of cancer cells, while at the same time maintaining a low incidence of side effects.

structure of the alternate allelic forms of the proteins, determinants can be identified which distinguish the allelic forms. Novel low molecular weight inhibitors or oligopeptides can then be designed for selective binding to these determinants and consequent allele-specific inhibition. Descriptions of targeted drug design can be found, for example, in I. Kuntz, Structure-Based Strategies

for Drug Design and Discovery, Science 257:1078-1082. . . have been described in Piper et
al., Studies Aided by Molecular Graphics of Effects of Structural Modifications
on the Binding of Antifolate Inhibitors to Human Dihydrofolate Reductase, Proc
Am. Assoc. Cancer Res. Annual Meeting 33:412 (1992); Hibert et al., Receptor
3D-Models and Drug Design, Therapie. . .

Low molecular weight inhibitors specific for each allelic protein form can be
predicted by molecular modeling and synthesized by standard organic chemistry
techniques. Computer modeling can. . .

The inhibitors of this invention can be identified by selecting those compounds
that selectively inhibit the growth of cells expressing one allelic form of a gene,
but do not inhibit the activity of the A allelic form.

B. Small Molecule Inhibitors
232/116
Low molecular weight inhibitors can be identified and generated by at least one of
the following methods; (1) screening of small organic molecules present in
microorganism. . .

Inhibition of protein function following differential binding. Several
mechanisms of inhibition are possible including.

competitive inhibition of active sites or critical allosteric sites,
allosteric inhibition of protein function,
altering compartmentalization or stability, and
inhibition of quaternary associations.

. . .
compounds that interact with
particular features of a polypeptide or protein or protein complex, There are clear
precedents for developing drugs, i.e., inhibitors, that are variance-specific
including drugs that are allosteric inhibitors of protein functions. Several lines of
experimental evidence demonstrate that small molecule variance specific
232/116
inhibitors can be designed and constructed for particular targets. Specifically.

Allosteric (noncompetitive) inhibition of protein function may be induced
by binding ligands to many different surfaces of a protein. Ligands can
cause allosteric inhibition by disturbing secondary, tertiary or quaternary
(subunit-subunit) interactions of a protein. There is ample evidence that
such effects can e induced by. . .

232/116
Competitive inhibitors can exert variance-specific effects by exhibiting
differential affinities for variant active sites, thereby interfering

with
binding of the substrate or critical allosteric. . .

Competitive inhibitors may bind with equal affinity for the
active site but
exerting different effects on the structure or function of the variant
domain.

Allosteric inhibitors can exert variance-specific effects by
binding
differentially to variant forms of the active domain and distorting the
structure or function of the. . .
. . .
model the topology and surface chemistry of the target
in detail. These data are useful in optimizing the binding specificity
or
allosteric inhibitory function of the product through a series
of iterative
steps once a prototype binding ligand is identified. Structural modeling
of
the target. . .

Sites of allosteric inhibition
Most drug development focuses on competitive inhibitors of
protein action rather
than noncompetitive, allosteric inhibitors. There is no a
priori advantage to a
competitive versus allosteric inhibitor except for the fact
that medicinal chemistry
often begins with candidate molecules derived from natural substrates or
cofactors. There are, in fact, conceptual advantages to allosteric
inhibitors since
each protein may contain multiple allosteric sites, and allosteric
inhibitors may be
effective at lower concentrations (e.g. those equivalent to the
substrate) since
there is no need to compete with the substrate. . .

Detailed crystallographic and other structural studies of a variety of
enzymes
show that the mechanism of allosteric inhibition commonly
involves
conforinational changes (e.g. domain movements) far from the site of
contact
with the allosteric regulator. These data illustrate the cooperativity.
. .
. . .
several well-characterized proteins. Another ~~is~~ to examine the
distribution of epitopes for antibodies that bind to the surface of a
protein and
inhibit its function. Analyses of these types show that
allosteric sites are widely
dispersed within proteins and may comprise the majority of. . .
. . .
Three HIV-1 RT structures have been published, including
complexes with double stranded DNA at 3.0 A resolution and with the non-
nucleoside inhibitors nevirapine (at 3.5A) and -APA (at 2.8A).

Two classes of HIV-1 RT inhibitors have been developed. The
first class
comprises nucleoside analogues including AZT, ddI and ddC. The second
class
comprises non-nucleoside analogues belonging to. . . 5 shows the
location of selected mutations within HIV-1
RT that cause resistance to nucleoside analogues as well as the

mechanism of
inhibition postulated from physical-chemical experiments and structural data; the
list is not comprehensive.

Table 4
232/116
Location and postulated mechanism of amino acid substitutions which confer
resistance to nucleoside analog inhibitors. trp266X - multiple substitutions.

analog resistance arises from mutations in
multiple domains. Many of the mutations are located far from the dNTP binding
sites. These changes inhibit drug function by altering the conformation of the
target protein in a manner analogous to those conformational changes that may be
induced by an allosteric inhibitor.

232/116
Table 5 summarizes the mutations that alter the function of non-nucleoside
inhibitor drugs
Table 5
Location and postulated mechanism of amino acid substitutions which confer
resistance to non-nucleoside analog inhibitors.

ala98gly 5b- 6 loop flexibility Pyridinone L-697661, Nevirapine
leul.00ile 5b- 6 loop -branch Pyridinone L-697661 Nevirapine, TIBO R82913
lyslolglu 5b- 6 loop charge Pyridinone. loop flexibility BHAP U-87201
lys238thr 14 charge BHAP U-87201
trp266X -thumb TIBO R82913
232/116
It is evident from these examples that the substitutions which inhibit drug functions
are distributed across several domains. Different inhibitory mechanisms have been
postulated in domains throughout the protein, based on the three-dimensional
structure of the protein. Most involve conforniational disruption of.

Thyrotropin receptor Naturally occurring antibodies against the thyrotropin
receptor can cause activation of thyroid function (Grave's disease) or inhibition of
thyroid function (Hashimoto's disease). The sites within the thyrotropin receptor
that are targeted by these natural antibodies have been mapped in detail and have
been tested with monoclonal antibodies. Most of the inhibitory antibodies do not
interfere with binding of thyrotropin to its receptor, and thus, are allosteric rather
than competitive inhibitors. Several independent classes of inhibitory antibodies
have been identified that bind to epitopes within different domains of the receptor.

can be deleted by site-directed mutagenesis without disrupting the function of the receptor. These experiments provide an explicit precedent for achieving allosteric inhibitory effects from ligands that target widely dispersed sequences within the protein.

Thermus aquaticus DNA polymerase The inhibitory activity of 24 monoclonal antibodies to Thermus aquaticus DNA polymerase has been investigated. The antibodies recognized 13 non-overlapping epitopes. Antibody binding to eight epitopes was inhibitory. Inhibitory antibodies mapped to several distinct domains, including the 5'nuclease domain, the polymerase domain and the boundary region between the 5'nuclease and polyinerase domains. Some antibodies recognized epitopes overlapping the DNA binding groove of the polymerase. Significantly, the inhibitory antibodies recognized epitopes constituting as much as 50% of the Taq polymerase surface, and the non-inhibitory antibodies a further -25%.

. . .

the pharmaceutical industry has worked to develop chemically modified penicillins and cephalosporins to elude inactivation by P-lactamases. In addition, a P-lactarnase inhibitor (clavulanic acid) has also been introduced into clinical use.

. . .

associated with drug resistance distributed evenly across the 740 amino acids of the protein. The mechanism by which some of these substitutions inhibit katG function can be inferred from the structure of the homologous yeast and E. coli enzymes and knowledge of the catalytic. . .

The application of small molecule inhibitor identification is specifically discussed in Example 39 below in connection with the methylguanine methyltransferase gene.

C. Antibody Inhibition.

Antibody inhibitors are most effective when they are directed against cell surface proteins or receptors. If the essential protein produced by the targeted allele is not a cell surface protein or receptor, the development of antibody inhibitors may also require the use of a special antibody-delivery system to facilitate entry of the antibody into the tumor cells. The plasma. . . the structure of the variable region of allele specific antibodies can be used as the basis for design of smaller allele specific inhibitory molecules.

. . .

receptors or other polypeptides essential for cell viability. Methods for screening peptide sequences

which have high specificity for binding to, and functional inhibition of, a specific polypeptide target have been well described previously. Scott, J.K. and Smith G.P., Searching for Peptide Ligands with an Epitope. . . by phage display of polypeptide sequences as well as direct screening of peptides or mixtures of synthetic peptides for binding to or inhibition of the target Rinctional polypeptide.

Ribozymes
Oligonucleotides or oligonucleotide analogs which interact with complementary sequences of cellular target DNA or RNA can be synthesized and used to inhibit or control gene expression at the levels of transcription or translation. The oligonucleotides of this invention can be either oligodeoxyribonucleotides or oligoribonucleotides, or. . . they can act enzymatically, such as ribozymes. Both antisense RNA and DNA can be used in this capacity as chemotherapeutic agents for inhibiting gene transcription or translation. Trojan, J., et aL, Treatment and prevention of rat glioblastoma, by immunogenic C6 cells expressing antisense insulin-like growth. . .

Inhibitory complementary oligonucleotides may be used as inhibitors for cancer therapeutics because of their high specificity and lack of toxicity.

Included in the scope of the invention are oligoribonucleotides, including antisense RNA and DNA molecules and ribozymes that function to inhibit expression of an essential gene in an allele specific manner. Anti-sense RNA and DNA molecules act to directly block the translation of. . .

A specific application of generating inhibitors which are either complementary oligonucleotides or inhibitory oligopeptides is described in Holzmayer, Pestov, and Roninson, Isolation of dominant negative mutants and inhibitory antisense RNA sequences by expression selection of random DNA fragments, Nucleic Acids Research 20:711-717 (1992). In this study, genetic suppressor elements (GSEs). . .

Preferred oligonucleotide inhibitors include oligonucleotide analogues which are resistant to degradation or hydrolysis by nucleases. These analogues include neutral, or nonionic, methylphosphonate analogues, which retain. . .

F, Gene Therapy
Nucleic acid molecules encoding oligonucleotide or polypeptide inhibitors will also be useftil in gene therapy (reviewed in Miller, Nature 357:455-460, (1992). Miller indicates that advances have resulted in practical approaches. . .

A nucleic acid sequence encoding an inhibitor may be administered utilizing an ex vivo approach

whereby cells are removed from an animal, transduced with the nucleic acid
sequence and reimplanted. . .

Many nonviral techniques for the delivery of a nucleic acid sequence encoding an
inhibitor into a cell can be used, including direct naked DNA uptake (e.g., Wolff et
al., Science 247: 1465-1468, 1990), receptor-mediated DNA. . .
. . .
its simplest form, gene transfer can be performed by simply injecting minute
amounts of DNA (e.g., a plasmid vector encoding an inhibitor) into the nucleus of a
cell, through a process of microinjection. Capecchi MR, Cell 22:479-88 (1980).

232/116
In another preferred embodiment, a vector having nucleic acid sequences encoding
an allele specific inhibitor is provided in which the nucleic acid sequence is
expressed only in specific tissue. Examples or methods of achieving tissue-specific
gene expression. . .

V11. Utility of allele-specific inhibitors of essential genes
A, Conditions susceptible to therapy.

The fraction of all cancers could be treated with allele specific inhibitors directed
against allele specific essential gene targets is a function of the frequency of the
target allele and the frequency of LOH.. . . exist in two allelic forms, each with an allele
frequency of 0.5 so that half the population would be heterozygous. An inhibitor of
one allele of such an ideal target would be a useful agent for 25% of all cancer
patients. An inhibitor of the other allele of the same ideal target would be
therapeutic for an additional 25% of all patients, making 50%. . .

Allele specific inhibitors of both alleles of such targets would be expected to
address 0.4 x 0.5 = 0.2 or 20% of the relevant. . .
<------User Break------>

```
=> s actin
         15854 ACTIN
           208 ACTINS
L24      15915 ACTIN
                (ACTIN OR ACTINS)

=> s stabil?
L25     282338 STABIL?

=> s ewing?
L26       3185 EWING?

=> s l26 and l24
L27       1098 L26 AND L24

=> s l27 and l25
L28       1004 L27 AND L25
```

```
=> s l24/ab
           151 ACTIN/AB
             1 ACTINS/AB
L29        152 (ACTIN/AB)
                ((ACTIN OR ACTINS)/AB)

=> s l29 and l26
L30          5 L29 AND L26

=> s l30 and l25
L31          5 L30 AND L25

=> d ibib 1-5

L31    ANSWER 1 OF 5     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2006029046 PCTFULL  ED 20060403  EW 200611
TITLE (ENGLISH):         USE OF LEPTIN IN WOUND HEALING
TITLE (FRENCH):          UTILISATION DE LEPTINE DANS LA GUERISON DE PLAIE
INVENTOR(S):             SIERRA-HONIGMANN, Maria Rocio, 656 Camino de la Luna,
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                         Street, Los Angeles, California 90017-2566;
                         90017-2566$; US
LANGUAGE OF FILING:      English
LANGUAGE OF PUBL.:       English
DOCUMENT TYPE:           Patent
PATENT INFORMATION:

                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 2006029046         A2 20060316

DESIGNATED STATES
       W:                AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO
                         CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR
                         HU ID IL IN IS JP KE KG KM KP KR KZ LC LK LR LS LT LU
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                         UG US UZ VC VN YU ZA ZM ZW
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                         LT LU LV MC NL PL PT RO SE SI SK TR
       RW (OAPI):        BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.:       WO 2005-US31455       A  20050902
PRIORITY INFO.:          US 2004-60607115         20040903

L31    ANSWER 2 OF 5     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2005042726 PCTFULL  ED 20050519  EW 200519
TITLE (ENGLISH):         METHODS FOR MODULATING AN IMMUNE RESPONSE BY MODULATING
                         KRC ACTIVITY
TITLE (FRENCH):          METHODES PERMETTANT DE MODULER UNE REPONSE IMMUNITAIRE
                         PAR MODULATION DE L'ACTIVITE DE KRC
INVENTOR(S):             GLIMCHER, Laurie, H., 51 Hampshire Street, West Newton,
                         MA 02165, US [US, US];
                         OUKKA, Mohamed, 46 Englewood Avenue, Brighton, MA
                         02146, US [US, US]
PATENT ASSIGNEE(S):      PRESIDENT AND FELLOWS OF HARVARD COLLEGE, 1350
                         Massachusetts Avenue, Suite 727, Cambridge, MA 02138,
                         US [US, US], for all designates States except US;
                         GLIMCHER, Laurie, H., 51 Hampshire Street, West Newton,
                         MA 02165, US [US, US], for US only;
                         OUKKA, Mohamed, 46 Englewood Avenue, Brighton, MA
                         02146, US [US, US], for US only
```

AGENT: DECONTI, Giulio, A.$, Lahive & Cockfield, LLP, 28 State Street, Boston, MA 02109$, US

LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2005042726	A2	20050512

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
RW (ARIPO): BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LU MC NL PL PT RO SE SI SK TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2004-US36641 A 20041103
PRIORITY INFO.: US 2003-10/701,401 20031103

L31 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2003027235 PCTFULL ED 20030410 EW 200314
TITLE (ENGLISH): AFAP SEQUENCES, POLYPEPTIDES, ANTIBODIES AND METHODS
TITLE (FRENCH): SEQUENCES AFAP, POLYPEPTIDES, ANTICORPS ET PROCEDES ASSOCIES
INVENTOR(S): FLYNN, Daniel, C., 418 Shawnee Drive, Morgantown, WV 26508-0911, US
PATENT ASSIGNEE(S): WEST VIRGINIA UNIVERSITY RESEARCH CORPORATION, P.O. Box 6216, 201 Chestnut Ridge Research Building, Morgantown, WV 26506-6216, US [US, US]
AGENT: SPAR, Elizabeth, N.$, Palmer & Dodge LLP, 111 Huntington Avenue, Boston, MA 02199-7613$, US

LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2003027235	A2	20030403

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2002-US29559 A 20020918
PRIORITY INFO.: US 2001-60/323,866 20010921

L31 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2002102846 PCTFULL ED 20030115 EW 200252
TITLE (ENGLISH): PHARMACEUTICAL COMPOSITION FOR DIAGNOSIS, PREVENTION OR TREATMENT OF A TUMOROUS STATE, COMPRISING A MODULATOR OF THE ACTIN POLYMERISATION STATE
TITLE (FRENCH): COMPOSITION PHARMACEUTIQUE POUR LE DIAGNOSTIC, LA PREVENTION OU LE TRAITEMENT D'UNE PATHOLOGIE TUMORALE, COMPRENANT UN AGENT MODULATEUR DE L'ETAT DE

POLYMERISATION DE L'ACTINE

INVENTOR(S): AUCLAIR, Christian, 22, avenue Parmentier, F-75011 Paris, FR [FR, FR];
AMSELLEM, Valerie, 103, avenue Philippe-Auguste, F-75011 Paris, FR [FR, FR];
HERVY, Martial, 5, rue de l'Amiral Mouchez, F-75013 Paris, FR [FR, FR];
SUBRA, Frederic, 3 bis, rue d'Athenes, F-75009 Paris, FR [FR, FR]

PATENT ASSIGNEE(S): BIOALLIANCE PHARMA, 59, rue du General Martial Valin, F-75015 Paris, FR [FR, FR], for all designates States except US;
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CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE -CNRS-, 3, rue Michel Ange, F-75794 Paris Cedex 16, FR [FR, FR], for all designates States except US;
AUCLAIR, Christian, 22, avenue Parmentier, F-75011 Paris, FR [FR, FR], for US only;
AMSELLEM, Valerie, 103, avenue Philippe-Auguste, F-75011 Paris, FR [FR, FR], for US only;
HERVY, Martial, 5, rue de l'Amiral Mouchez, F-75013 Paris, FR [FR, FR], for US only;
SUBRA, Frederic, 3 bis, rue d'Athenes, F-75009 Paris, FR [FR, FR], for US only

AGENT: BRESSE, Pierre$, Bresse-Majerowicz, 3, avenue de l'Opera, F-75001 Paris$, FR

LANGUAGE OF FILING: French
LANGUAGE OF PUBL.: French
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002102846	A2	20021227

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-FR2106 A 20020618
PRIORITY INFO.: FR 2001-01/07976 20010618

L31 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999022028 PCTFULL ED 20020515
TITLE (ENGLISH): MODULATORS OF ACTIN
TITLE (FRENCH): MODULATEURS D'ACTINE
INVENTOR(S): KING, Mary-Claire;
LYNCH, Eric, D.;
LEE, Ming, K.;
MORROW, Jan, E.;
WELCSH, Piri, L.;
LEON, Pedro, E.

PATENT ASSIGNEE(S): THE UNIVERSITY OF WASHINGTON;
THE UNIVERSITY OF COSTA RICA

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9922028	A1	19990506

DESIGNATED STATES
W: CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.:	WO 1998-US23024	A	19981029
PRIORITY INFO.:	US 1997-60/063,737		19971029
	US 1998-09/080,897		19980518

=> d kwic 31
5 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
The answer numbers requested are not in the answer set.
ENTER ANSWER NUMBER OR RANGE (1):eng
ANSWER NUMBERS NOT CORRECTLY SPECIFIED
Enter an answer number, Example: 10
several answer numbers, Example: 3,7,10
a range of answer numbers, Example: 5-10
or a combination of these. Example: 3,7,9-10,15
ENTER ANSWER NUMBER OR RANGE (1):end

=> d kwic 3

L31 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ABEN The present invention comprises reagents and methods which target actin filaments or the cellular signals that control actin filament integrity. Specifically, the invention provides novel actin binding polypeptides (e.g., human AFAP polypeptides), antibodies which specifically recognize the same, nucleic acids encoding the same, and methods for. . .

DETD . . . aspect, the pathology is cancer, e.g., such as breast cancer, colon cancer,
prostate cancer, lung cancer, a cancer involving neural cells, Ewing sarcoma and
rhabdomyosarcoma.

. . .
acids comprising one or more of modified bases, sugars, and intermicleotide linkages
which preferably have the substantially the same or enhanced stability and/or specificity for a
target nucleic acid as the nucleic acids from which they are derived.

. . .
Antisense nucleic acids can also be
chemically synthesized and can be deoxynucleotides or modified forms thereof which are
selected to have enhanced stability in vivo.

. . .
activated in a number of human cancers including breast cancer, colon cancer, prostate cancer, lung cancer (e.g., small lung cell carcinoma), neuroblastoma,
Ewing sarcoma and rhabdomyosarcoma (Cartwright et al., 1990, supra; Rosen et al., 1986,
supra).

. . .
breast cancer, colon cancer, prostate cancer, lung cancer
(e.g., small lung cell carcinoma), a cancer involving neural cells (e.g., such as neuroblastoma),
Ewing sarcoma and rhabdomyosarcoma.

. . .
forms thereof. In one aspect, the condition is cancer (e.g., such as breast cancer, colon cancer, prostate cancer, lung cancer,

neuroblastoma, Ewing sarcoma
and rhabdomyosarcoma). In another aspect, the condition is a
neurological disease (which can
47
The agents, agonists, and antagonists may be formulated. . .
. . .
and coverslips and observed under confocal microscopy (Zeiss,
Oberkochen, Germany). Samples for negative staining were adsorbed to
grids coated with
nitrocellulose and stabilized with carbon (Ernest F. Fullam,
Latham, NY). Unbound protein was
removed by successive washes with buffer and water before staining with.
. .

CLMEN. . . said cancer is selected from the group
consisting of. breast cancer, colon cancer, prostate cancer, lung
cancer, a cancer
involving neural cells, Ewing sarcoma and rhabdomyosarcoma.

=> d kwic 5

L31 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ABEN The invention provides methods and compositions which find use, i(inter
alia), for modulating
the stabilization of actin filaments. The
compositions may comprise one or more polypeptide moieties
derived from a novel human diaphanous polypeptide and/or one or. . .
ABFR L'invention concerne des procedes et des compositions permettant, entre
autres choses, de
moduler la stabilisation des filaments d'actine. Ces
compositions peuvent comprendre une ou
plusieurs fractions de polypeptide derivees d'un nouveau polypeptide
diaphane de l'homme. . .

DETD INTRODUCTION
Field of the Invention
The invention relates to a class of polypeptides involved in actin
stabilization.
. . .
of the Invention
The actin cytoskeleton plays a central role in defining cellular
structure and effecting
dynamic changes in morphology. By selectively stabilizing and
destabilizing actin
polymerization, the cell is able to effect a wide range of structural
reorganization and effect
phenomena such as cell. . .

the progress of many pathogenic infections, invasion and metastisis of
neoplasia, fertilization,
clotting and wound repair, etc., the stability of actin
polymerization is a choice target for
therapuetic intervention. In fact, potent drugs effecting actin filament
destabilization and
stabilization such as fungal-derived alkaloids including the
cytochalasins and phalloidins are
well known. Here we disclose a new family of modulators of actin polymer
stabilization
derived from a novel human diaphanous protein and gene.

SUMMARY OF THE INVENTION
The invention provides methods and compositions which find use. inter
alia, for
modulating the stabilization of actin filaments. The

compositions may comprise one or more
polypeptide moieties derived from a novel human diaphanous polypeptide
and/or one. . .

. . .
other polypeptide moieties, complexed in a wide variety of
covalent and/or non-covalent associations and binding complexes, etc.,
which may provide
enhanced activity, stability, availability, targeting, etc.

. . .
polypeptide
hDial-del-15: CYCLIN B2 - residues 1141-1171 of SEQ ID NO:2 fusion
polypeptide
The invention provides methods and compositions of selectively
modulating
cytoskeletal de/stabilization and/or the effective
concentration of a human diaphanous protein
within a target cell. The general methods involve introducing into the
target. . . the human diaphanous polypeptide moiety, the modulator
may
comprise a wide variety of additional moieties, including moieties which
provide for
detection, targeting, stability, proteolytic resistance, etc.
Preferred modulators demonstrate
cytoskelatal de/stabilization with several alternative methods
of introduction, including direct
medium uptake, uptake facilitated by chaotropic agents including
detergents (e.g. TWEEN20,
etc.), guanadine salts,. . .

. . .
to a probe specific for the binding agent. Agents of
particular interest modulate human diaphanous polypeptide function, e.g.
human diaphanous
5
polypeptide-dependent actin de/stabilization.

. . .
usually RNA or DNA, it is often advantageous to use nucleic acids
comprising other bases or nucleotide analogs to provide modified
stability, etc.

. . .
3.0 were transferred to a UNIX-based Sun workstation for cont-ig'
assembly and blast analysis. The computer program PHRED (Green P and
Ewing B. 1996.

. . .
phrap.docs/ phred.html) was used to assign bases
to the electropherograms. After eliminating vector sequences, the
program PHRAP (Green P
1 0 and Ewing B. 1996. http:H www.bozeman.mbt.washington.edu/
phrap.docs/ phrap.html) was
used to analyze the sequences, identify overlapping individual
sequences, and assemble them
into contigs. To. . .

. . .
daily blood and peritoneal sample to evaluate peritoneal fluid cell
counts,
hernatological cell counts, serum chemistries, bacterial cultures as
needed, vector stability,
viral uptake by cells, expression of hDial gene and presence of
antibodies to vector envelope
proteins. At four week intervals patients are. . .

Detection of vector stability and expression. DNA is prepared
from cell samples by
hypotonic lysis, digestion with proteinase K (Boehringer Mannheim,
Indianapolis. Indiana)
and SDS, followed. . .

PCR primers specific for the neo sequences within the LXSN-hDialsv vector are
employed for determination of vector presence and stability within patient samples. RT-PCR
is performed by our published methods (Thompson, M. E., et al. Nature Genetics 9, 444-
450] 1995.).

```
=> s ewing sarcoma or (ewing? sarcoma
UNMATCHED LEFT PARENTHESIS 'OR (EWING?'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s ewing sarcoma or (ewing?(sarcoma)
          3035 EWING
           132 EWINGS
          3112 EWING
                 (EWING OR EWINGS)
         18118 SARCOMA
          5088 SARCOMAS
             5 SARCOMATA
         19804 SARCOMA
                 (SARCOMA OR SARCOMAS OR SARCOMATA)
           392 EWING SARCOMA
                 (EWING(W)SARCOMA)
          3185 EWING?
         18118 SARCOMA
          5088 SARCOMAS
             5 SARCOMATA
         19804 SARCOMA
                 (SARCOMA OR SARCOMAS OR SARCOMATA)
           400 EWING? SARCOMA
                 (EWING?(W)SARCOMA)
L32        400 EWING SARCOMA OR (EWING? SARCOMA)

=> d his

     (FILE 'HOME' ENTERED AT 14:41:45 ON 17 APR 2006)

     FILE 'REGISTRY' ENTERED AT 14:41:55 ON 17 APR 2006
                E "DOLASTATIN"/CN 25
L1            1 S E6

     FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006
L2        52669 S ACTIN
L3          812 S COFILIN
L4      1968300 S ANTAG? OR INHIBIT?
L5          222 S L4 (L) L3
L6         1659 S EWING?
L7            1 S L6 AND L5
L8           22 S L1
L9            0 S L8 AND L6
L10         224 S ZYXIN
L11           3 S L10 AND L6
L12           6 S L3 AND L6
L13           4 S L12 AND L4
L14         989 S PHOSPHOINOSITOL?
L15           0 S L14 AND L6
L16          98 S PHOSPHOTIDYLINOSITOL
L17           0 S L15 AND L6

     FILE 'PCTFULL' ENTERED AT 14:49:15 ON 17 APR 2006
L18         188 S COFILIN
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L19         3185 S EWING?
L20           19 S L19 AND L18
L21       198141 S ANTAG? OR INHIBIT?
L22           19 S L20 AND L21
L23            4 S L22 NOT PY>2001
L24        15915 S ACTIN
L25       282338 S STABIL?
L26         3185 S EWING?
L27         1098 S L26 AND L24
L28         1004 S L27 AND L25
L29          152 S L24/AB
L30            5 S L29 AND L26
L31            5 S L30 AND L25
L32          400 S EWING SARCOMA OR (EWING? SARCOMA)

=> s l32 and l24
L33          165 L32 AND L24

=> s l33 and l25
L34          137 L33 AND L25

=> s l34 not py>2001
        488865 PY>2001
L35           54 L34 NOT PY>2001

=> s l35 and l29
L36            0 L35 AND L29

=> s l24/clm
L37         1198 (ACTIN/CLM)

=> s l37 and l35
L38            5 L37 AND L35

=> s l24/ti
L39           44 (ACTIN/TI)

=> s l39 and l35
L40            0 L39 AND L35

=> d ibib l38 1-5

L38    ANSWER 1 OF 5      PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2001055368 PCTFULL  ED 20020827
TITLE (ENGLISH):         NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH):          ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S):             ROSEN, Craig, A.;
                         BARASH, Steven, C.;
                         RUBEN, Steven, M.
PATENT ASSIGNEE(S):      HUMAN GENOME SCIENCES, INC.;
                         ROSEN, Craig, A.;
                         BARASH, Steven, C.;
                         RUBEN, Steven, M.
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 2001055368        A1 20010802
DESIGNATED STATES
       W:                AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
                         CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
                         IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
                         MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
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                         SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
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DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-US1348 A 20010117
PRIORITY INFO.: US 2000-60/179,065 20000131
US 2000-60/180,628 20000204
US 2000-60/184,664 20000224
US 2000-60/186,350 20000302
US 2000-60/189,874 20000316
US 2000-60/190,076 20000317
US 2000-60/198,123 20000418
US 2000-60/205,515 20000519
US 2000-60/209,467 20000607
US 2000-60/214,886 20000628
US 2000-60/215,135 20000630
US 2000-60/216,647 20000707
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US 2000-60/217,487 20000711
US 2000-60/217,496 20000711
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US 2000-60/220,963 20000726
US 2000-60/220,964 20000726
US 2000-60/225,757 20000814
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US 2000-60/225,447 20000814
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US 2000-60/231,244 20000908
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US 2000-60/234,274 20000921

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US 2000-60/235,836	20000927
US 2000-60/236,369	20000929
US 2000-60/236,327	20000929
US 2000-60/236,370	20000929
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US 2000-60/249,264	20001117
US 2000-60/249,209	20001117
US 2000-60/249,300	20001117
US 2000-60/249,265	20001117
US 2000-60/250,391	20001201
US 2000-60/250,160	20001201
US 2000-60/256,719	20001205
US 2000-60/251,030	20001205

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US 2000-60/251,869 20001208
US 2000-60/251,856 20001208
US 2000-60/251,868 20001208
US 2000-60/251,990 20001208
US 2000-60/251,989 20001208
US 2000-60/254,097 20001211
US 2001-60/259,678 20010105

L38 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001055328 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055328	A2	20010802

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
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APPLICATION INFO.:	WO 2001-US1359	A	20010117
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US 2000-60/251,990	20001208
US 2000-60/251,989	20001208
US 2000-60/254,097	20001211
US 2001-60/259,678	20010105

L38 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001055201 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055201	A1	20010802

DESIGNATED STATES
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TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD

SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
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APPLICATION INFO.:
WO 2001-US1317 A 20010117

PRIORITY INFO.:
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US 2000-60/184,664 20000224
US 2000-60/186,350 20000302
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US 2000-60/254,097 20001211
US 2001-60/259,678 20010105

L38 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001054733 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
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SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
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APPLICATION INFO.:	WO 2001-US1312	A	20010117
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US 2000-60/254,097	20001211
US 2001-60/259,678	20010105

L38 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 2001053514 PCTFULL ED 20020827

TITLE (ENGLISH): TOXICANT-INDUCED DIFFERENTIAL GENE EXPRESSION

TITLE (FRENCH): EXPRESSION GENETIQUE DIFFERENTIELLE INDUITE PAR SUBSTANCES TOXIQUES

INVENTOR(S): REIDHAAR-OLSON, John, F.

PATENT ASSIGNEE(S): GLAXO GROUP LIMITED;
REIDHAAR-OLSON, John, F.

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001053514	A1	20010726

DESIGNATED STATES
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APPLICATION INFO.:       WO 2001-US1920       A  20010119
PRIORITY INFO.:          US 2000-09/489,220      20000121


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Executing the logoff script...

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Connecting via Winsock to STN



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LOGINID:SSSPTA1642BJF

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  DEC 23  New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
                  USPAT2
 NEWS  4  JAN 13  IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
 NEWS  5  JAN 13  New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
                  INPADOC
 NEWS  6  JAN 17  Pre-1988 INPI data added to MARPAT
 NEWS  7  JAN 17  IPC 8 in the WPI family of databases including WPIFV
 NEWS  8  JAN 30  Saved answer limit increased
 NEWS  9  FEB 21  STN AnaVist, Version 1.1, lets you share your STN AnaVist
                  visualization results
 NEWS 10  FEB 22  The IPC thesaurus added to additional patent databases on STN
 NEWS 11  FEB 22  Updates in EPFULL; IPC 8 enhancements added
 NEWS 12  FEB 27  New STN AnaVist pricing effective March 1, 2006
 NEWS 13  FEB 28  MEDLINE/LMEDLINE reload improves functionality
 NEWS 14  FEB 28  TOXCENTER reloaded with enhancements
 NEWS 15  FEB 28  REGISTRY/ZREGISTRY enhanced with more experimental spectral
                  property data
 NEWS 16  MAR 01  INSPEC reloaded and enhanced
 NEWS 17  MAR 03  Updates in PATDPA; addition of IPC 8 data without attributes
 NEWS 18  MAR 08  X.25 communication option no longer available after June 2006
 NEWS 19  MAR 22  EMBASE is now updated on a daily basis
 NEWS 20  APR 03  New IPC 8 fields and IPC thesaurus added to PATDPAFULL
 NEWS 21  APR 03  Bibliographic data updates resume; new IPC 8 fields and IPC
                  thesaurus added in PCTFULL
 NEWS 22  APR 04  STN AnaVist $500 visualization usage credit offered
 NEWS 23  APR 12  LINSPEC, learning database for INSPEC, reloaded and enhanced
 NEWS 24  APR 12  Improved structure highlighting in FQHIT and QHIT display
                  in MARPAT
 NEWS 25  APR 12  Derwent World Patents Index to be reloaded and enhanced during
                  second quarter; strategies may be affected
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 NEWS EXPRESS  FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
               V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
               http://download.cas.org/express/v8.0-Discover/

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 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

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specific topic.

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  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:12:12 ON 17 APR 2006

=> file pctfull
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                      0.21       0.21

FILE 'PCTFULL' ENTERED AT 16:12:30 ON 17 APR 2006
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FILE LAST UPDATED:          11 APR 2006      <20060411/UP>
MOST RECENT UPDATE WEEK:        200614        <200614/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
    SEE
    http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE
    (last updated April 10, 2006) <<<

=> s jasplakinolide
           171 JASPLAKINOLIDE
             1 JASPLAKINOLIDES
L1         171 JASPLAKINOLIDE
                 (JASPLAKINOLIDE OR JASPLAKINOLIDES)

=> s ewing? (2W) sarcoma
          3185 EWING?
         18118 SARCOMA
          5088 SARCOMAS
             5 SARCOMATA
         19804 SARCOMA
                 (SARCOMA OR SARCOMAS OR SARCOMATA)
L2        1574 EWING? (2W) SARCOMA

=> s l2 and l1
L3          36 L2 AND L1

=> s l3 not py>2001
        488865 PY>2001
```

L4 1 L3 NOT PY>2001

=> d ibib

L4 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2000071135 PCTFULL ED 20020515
TITLE (ENGLISH): ANTI-TUMOR COMPRISING BOROPROLINE COMPOUNDS
TITLE (FRENCH): AGENTS ANTI-TUMORALES CONTENANT DES COMPOSES DE BOROPROLINE
INVENTOR(S): WALLNER, Barbara, P.;
MILLER, Glenn
PATENT ASSIGNEE(S): POINT THERAPEUTICS, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000071135	A1	20001130

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ
TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK
ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM
GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:	WO 2000-US14505	A	20000525
PRIORITY INFO.:	US 1999-60/135,861		19990525

=> d kwic

L4 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . myxoid liposarcomas and pleiomorphic
liposarcomas), leiomyosarcomas, rhabdomyosarcomas, malignant peripheral nerve sheath
tumors (also called malignant schwannomas, neurofibrosarcomas, or neurogenic sarcomas),
Ewing's tumors (including Ewing's sarcoma of bone,
extraskeletal [not bone] Ewing's
io sarcoma, and primitive neuroectoderinal tumor [PNET]),
synovial sarcoma, angiosarconias,
hemangiosarcomas, lymphangiosarcomas, Kaposi's sarcoma,
hemangioendothelioma,
fibrosarcoma, desmoid tumor (also called aggressive fibromatosis),
dermatofibrosarcoma
protuberans (DFSP),. . .
. . .
immunostimulant peptides-, insulin-like growth factor-I receptor
inhibitoi, interferon
agonists; interferons; interleukins; iobenguane; lododoxorubicin;
1porneanol, 4-; irinotecan;
iroplact; irsogladine; isobengazole; ischomohalicondrin B; itasetron;
jasplakinolide;
kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin;
lenograstim; lentinan sulfate;
leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha
interferon; leuprolide +
estrogen + progesterone; leuprorelin;. . .

=> s hepatocarcinoma? or mesenchymal or neuroectodermal
463 HEPATOCARCINOMA?

```
          4765 MESENCHYMAL
             1 MESENCHYMALS
          4765 MESENCHYMAL
                 (MESENCHYMAL OR MESENCHYMALS)
           922 NEUROECTODERMAL
             1 NEUROECTODERMALS
           922 NEUROECTODERMAL
                 (NEUROECTODERMAL OR NEUROECTODERMALS)
L5        5608 HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL

=> s l5 and l4
L6           1 L5 AND L4

=> d kwic\
'KWIC\' IS NOT A VALID FORMAT FOR FILE 'PCTFULL'

The following are valid formats:

ALL, MAX--------BIB plus IND plus ABS plus TX
ALLG------------ALL, MAX plus GI
BIB-------------AN, ED, UP, EW, UW, TIEN, TIFR, TIDE, TIES, IN, PA, LA, LAF
                DT, PI, DS, AI, PRAI
BIBG------------BIB plus GI
IND, IPC--------ICM, ICS
ABS-------------ABEN, ABF, ABFR, ABDE, ABES
TX--------------DETD, CLM
IALL,IMAX-------ALL indented with text labels
IALLG,IMAXG-----IALL, IMAX plus GI
DALL------------Delimited ALL format
STD-------------BIB plus IND
STDG------------STD plus GI
ISTD------------STD indented with text labels
ISTDG-----------ISTD plus GI
BRIEF-----------BIB plus ABS
BRIEFG----------BIB plus ABS plus GI
IBRIEF----------BRIEF indented with text labels
IBRIEFG---------IBRIEF plus GI
SCAN------------TI (random display without AN)
TRIAL (TRI)-----FA, TI, CLMN, DETN
SAMPLE (SAM)----FA, TI, CLMN, DETN
FREE------------FA, TI, CLMN, DETN
ENTER DISPLAY FORMAT (STD):kwic

L6     ANSWER 1 OF 1     PCTFULL   COPYRIGHT 2006 Univentio on STN

DETD  . . . epithelium eductus semicircularis, enamel epithelium, false
       epithelium,
       germinal epithelium, gingival epithelium, glandular epithelium,
       glomerular epithelium,
       laminated epithelium, epithelium of lens, epithelium lentis,
       mesenchymal epithelium,
       olfactory epithelium, pavement epithelium, pigmentary epithelium,
       pigmented epithelium,
       protective epithelium, pseudostratified epithelium, pyramidal
       epithelium, respiratory
       epithelium, rod epithelium, serniniferous epithelium, sense epithelium,.
       . .
 . . .
       gelatinous carcinoma, giant cell
       carcinoma, gigantocellulare, glandular carcinoma, granulosa. cell
       carcinoma, hair-matrix
       carcinoma, hematoid carcinoma, hepatocellular carcinoma (also called
       hepatoma, malignant
       hepatoma and hepatocarcinoma), Mirthle cell carcinoma, hyaline
       carcinoma, hypernephroid
```

carcinoma, infantile embryonal carcinoma, carcinoma in situ, intraepidermal carcinoma,
intraepithelial carcinoma, Krompecher's carcinoma, Kulchitzky-cell carcinoma, lenticular
carcinoma,. . .
. . .
characterized by an abnormal mammalian cell proliferation to be treated by the methods of the invention include sarcomas. Sarcomas are rare mesenchymal
neoplasms that arise in bone and soft tissues. Different types of sarcomas are recognized and
these include: liposarcomas (including myxoid liposarcomas and pleiomorphic
liposarcomas), leiomyosarcomas, rhabdomyosarcomas, malignant peripheral nerve sheath
tumors (also called malignant schwannomas, neurofibrosarcomas, or neurogenic sarcomas),
Ewing's tumors (including Ewing's sarcoma of bone,
extraskeletal [not bone] Ewing's
io sarcoma, and primitive neuroectoderinal tumor [PNET]),
synovial sarcoma, angiosarconias,
hemangiosarcomas, lymphangiosarcomas, Kaposi's sarcoma,
hemangioendothelioma,
fibrosarcoma, desmoid tumor (also called aggressive fibromatosis),
dermatofibrosarcoma
protuberans (DFSP),. . .
. . .
immunostimulant peptides-, insulin-like growth factor-I receptor inhibitoi, interferon
agonists; interferons; interleukins; iobenguane; lododoxorubicin; lporneanol, 4-; irinotecan;
iroplact; irsogladine; isobengazole; isohomohalicondrin B; itasetron; jasplakinolide;
kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin;
lenograstim; lentinan sulfate;
leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha interferon; leuprolide +
estrogen + progesterone; leuprorelin;. . .

```
=> d his

     (FILE 'HOME' ENTERED AT 16:12:12 ON 17 APR 2006)

     FILE 'PCTFULL' ENTERED AT 16:12:30 ON 17 APR 2006
L1          171 S JASPLAKINOLIDE
L2         1574 S EWING? (2W) SARCOMA
L3           36 S L2 AND L1
L4            1 S L3 NOT PY>2001
L5         5608 S HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL
L6            1 S L5 AND L4

=> s l5 and l1
L7           37 L5 AND L1

=> s l7 not py>2001
        488865 PY>2001
L8            4 L7 NOT PY>2001

=> d ibib 1-4

L8     ANSWER 1 OF 4      PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2001089520 PCTFULL  ED 20020826
TITLE (ENGLISH):         DEHYDROASCORBIC ACID FORMULATIONS AND USES THEREOF
TITLE (FRENCH):          FORMULATIONS D'ACIDE DEHYDROASCORBIQUE ET LEURS
```

UTILISATIONS

INVENTOR(S): OLSON, William, C.;
ISRAEL, Robert, J.;
BOYD, Thomas, A.

PATENT ASSIGNEE(S): PROGENICS PHARMACEUTICALS, INC.;
OLSON, William, C.;
ISRAEL, Robert, J.;
BOYD, Thomas, A.

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001089520	A2	20011129

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US41407 A 20001020
PRIORITY INFO.: US 2000-60/205,870 20000519

L8 ANSWER 2 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001029235 PCTFULL ED 20020820
TITLE (ENGLISH): TMS1 COMPOSITIONS AND METHODS OF USE
TITLE (FRENCH): COMPOSITIONS DU GENE TMS1 ET PROCEDES D'UTILISATION
INVENTOR(S): VERTINO, Paula, M.
PATENT ASSIGNEE(S): EMORY UNIVERSITY
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001029235	A2	20010426

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.: WO 2000-US28747 A 20001018
PRIORITY INFO.: US 1999-60/159,975 19991018

L8 ANSWER 3 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2000071135 PCTFULL ED 20020515
TITLE (ENGLISH): ANTI-TUMOR COMPRISING BOROPROLINE COMPOUNDS
TITLE (FRENCH): AGENTS ANTI-TUMORALES CONTENANT DES COMPOSES DE BOROPROLINE
INVENTOR(S): WALLNER, Barbara, P.;
MILLER, Glenn
PATENT ASSIGNEE(S): POINT THERAPEUTICS, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000071135	A1	20001130

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US14505 A 20000525
PRIORITY INFO.: US 1999-60/135,861 19990525

L8 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999004817 PCTFULL ED 20020515
TITLE (ENGLISH): CHEMOTHERAPY SYNERGISTIC AGENT
TITLE (FRENCH): AGENT SYNERGIQUE POUR CHIMIOTHERAPIE
INVENTOR(S): WINKELMAN, James, W.;
BRIDGES, Kenneth, R.
PATENT ASSIGNEE(S): BRIGHAM & WOMEN'S HOSPITAL, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9904817	A1	19990204

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-US15052 A 19980722
PRIORITY INFO.: US 1997-60/053,696 19970725
US 1997-60/054,148 19970725

=> d kwic 4

L8 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . 91)
-
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcorna and osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basal. . .
. . .
peptides; insulin-like
growth factor-I receptor inhibitor; interferon agonists; interferons; interleukins; iobenguane;
I 0 iododoxorubicin; ipomeanol, 4-; irinotecan; iroplact; irsogladine; isobengazole;
isohomohalicondrin B; itasetron; jasplakinolide; kahalalide F;
larnellarin-N triacetate;
lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin; letrozole; leukemia
inhibiting factor; leukocyte alpha interferon; leuprolide + estrogen + progesterone;
leuprorelin;. . .

CLMEN. . . and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas, including
leiornyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basocellular. . .
. . .
and

lymphocytic lymphomas; neuroblastomas; oral cancer, including squarnous cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin
- 24 -
cancer, including melanoma, Kaposi's. . .
. . .
and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer'; rectal cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basocellular. . .

=> file caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	15.65	15.86

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FILE COVERS 1907 - 17 Apr 2006 VOL 144 ISS 17
FILE LAST UPDATED: 16 Apr 2006 (20060416/ED)

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http://www.cas.org/infopolicy.html

=> s jasplakinolide/cn
REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L10 118 L9

=> s jasplakinolide

```
           251 JASPLAKINOLIDE
             1 JASPLAKINOLIDES
L11        252 JASPLAKINOLIDE
                 (JASPLAKINOLIDE OR JASPLAKINOLIDES)

=> s l11 or l10
L12        279 L11 OR L10

=> s hepatocarcinoma? or mesenchymal or neuroectodermal
          1409 HEPATOCARCINOMA?
         11238 MESENCHYMAL
          1281 NEUROECTODERMAL
L13      13848 HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL

=> s l13 and l12
L14           2 L13 AND L12

=> d ibib 1-2

L14  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2005:248055  CAPLUS
DOCUMENT NUMBER:         142:352644
TITLE:                   RhoA/ROCK Signaling Regulates Sox9 Expression and
                         Actin Organization during Chondrogenesis
AUTHOR(S):               Woods, Anita; Wang, Guoyan; Beier, Frank
CORPORATE SOURCE:        Canadian Institutes of Health Research Group in
                         Skeletal Development and Remodeling, Department of
                         Physiology and Pharmacology, University of Western
                         Ontario, London, ON, N6A 5C1, Can.
SOURCE:                  Journal of Biological Chemistry (2005), 280(12),
                         11626-11634
                         CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER:               American Society for Biochemistry and Molecular
                         Biology
DOCUMENT TYPE:           Journal
LANGUAGE:                English
REFERENCE COUNT:         73    THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2003:816528  CAPLUS
DOCUMENT NUMBER:         140:12638
TITLE:                   Two CD95 tumor classes with different sensitivities to
                         antitumor drugs
AUTHOR(S):               Algeciras-Schimnich, Alicia; Pietras, Eric M.;
                         Barnhart, Bryan C.; Legembre, Patrick; Vijayan,
                         Shrijay; Holbeck, Susan L.; Peter, Marcus E.
CORPORATE SOURCE:        The Ben May Institute for Cancer Research, University
                         of Chicago, Chicago, IL, 60637, USA
SOURCE:                  Proceedings of the National Academy of Sciences of the
                         United States of America (2003), 100(20), 11445-11450
                         CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:               National Academy of Sciences
DOCUMENT TYPE:           Journal
LANGUAGE:                English
REFERENCE COUNT:         26    THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> s ewing? (2W) sarcoma
          1659 EWING?
         36667 SARCOMA
          4162 SARCOMAS
           100 SARCOMATA
         38298 SARCOMA
```

```
                (SARCOMA OR SARCOMAS OR SARCOMATA)
L15       1277 EWING? (2W) SARCOMA

=> s l15 and l12
L16          0 L15 AND L12

=> s dolastatin 11/cn
   REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.



L18         22 L17

=> s dolastatin 11
           390 DOLASTATIN
            59 DOLASTATINS
           404 DOLASTATIN
                 (DOLASTATIN OR DOLASTATINS)
        916607 11
L19         22 DOLASTATIN 11
                 (DOLASTATIN(W)11)

=> s l19 or l18
L20         24 L19 OR L18

=> d his

     (FILE 'HOME' ENTERED AT 16:12:12 ON 17 APR 2006)

     FILE 'PCTFULL' ENTERED AT 16:12:30 ON 17 APR 2006
L1           171 S JASPLAKINOLIDE
L2          1574 S EWING? (2W) SARCOMA
L3            36 S L2 AND L1
L4             1 S L3 NOT PY>2001
L5          5608 S HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL
L6             1 S L5 AND L4
L7            37 S L5 AND L1
L8             4 S L7 NOT PY>2001

     FILE 'CAPLUS' ENTERED AT 16:18:34 ON 17 APR 2006
                 S JASPLAKINOLIDE/CN

     FILE 'REGISTRY' ENTERED AT 16:18:43 ON 17 APR 2006
L9             1 S JASPLAKINOLIDE/CN

     FILE 'CAPLUS' ENTERED AT 16:18:43 ON 17 APR 2006
L10          118 S L9
L11          252 S JASPLAKINOLIDE
L12          279 S L11 OR L10
L13        13848 S HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL
L14            2 S L13 AND L12
L15         1277 S EWING? (2W) SARCOMA
L16            0 S L15 AND L12
                 S DOLASTATIN 11/CN

     FILE 'REGISTRY' ENTERED AT 16:20:17 ON 17 APR 2006
L17            1 S DOLASTATIN 11/CN

     FILE 'CAPLUS' ENTERED AT 16:20:18 ON 17 APR 2006
L18           22 S L17
```

```
L19           22 S DOLASTATIN 11
L20           24 S L19 OR L18

=> s l20 and l13
L21           1 L20 AND L13

=> d ibib

L21  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2003:816528  CAPLUS
DOCUMENT NUMBER:          140:12638
TITLE:                    Two CD95 tumor classes with different sensitivities to
                          antitumor drugs
AUTHOR(S):                Algeciras-Schimnich, Alicia; Pietras, Eric M.;
                          Barnhart, Bryan C.; Legembre, Patrick; Vijayan,
                          Shrijay; Holbeck, Susan L.; Peter, Marcus E.
CORPORATE SOURCE:         The Ben May Institute for Cancer Research, University
                          of Chicago, Chicago, IL, 60637, USA
SOURCE:                   Proceedings of the National Academy of Sciences of the
                          United States of America (2003), 100(20), 11445-11450
                          CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:                National Academy of Sciences
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          26    THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d kwic

L21  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
AB    . . . half are type II. Most of the type I cell lines fall into a
      distinct class of tumor cells expressing mesenchymal-like genes,
      whereas the type II cell lines preferentially express epithelium-like
      markers. This suggests that type I and II tumor cells represent different
      stages of carcinogenesis that resemble the epithelial-mesenchymal
      transition. We then screened the National Cancer Institute database of
      >42,000 compds. for reagents with patterns of growth inhibition that.
      .
ST    soluble CD95ligand antitumor mesenchymal epithelial tumor actin
      tubulin disruption; antitumor resistance CD95 signaling gene expression
      carcinogenesis
IT    362-07-2, 2-Methoxyestradiol   1110-02-7, NSC 112167   2222-07-3,
      Cucurbitacin I   6040-19-3, Cucurbitacin A   6766-43-4, Cucurbitacin K
      33069-62-4D, Taxol, analog   82855-09-2D, Combretastatin, analog
      102396-24-7D, Jasplakinolide, analog   108675-64-5 111517-68-1,
      NSC 606195   141172-06-7   630400-59-8, NSC 666608   630400-60-1, NSC
      658831   630400-62-3, NSC 666606
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
         (two CD95 tumor classes with different sensitivities to antitumor
         drugs)


=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y
```

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	8.35	50.43

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.75	-0.75

STN INTERNATIONAL LOGOFF AT 16:21:51 ON 17 APR 2006

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1642BJF

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 8	JAN 30	Saved answer limit increased
NEWS 9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 14	FEB 28	TOXCENTER reloaded with enhancements
NEWS 15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 16	MAR 01	INSPEC reloaded and enhanced
NEWS 17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 18	MAR 08	X.25 communication option no longer available after June 2006
NEWS 19	MAR 22	EMBASE is now updated on a daily basis
NEWS 20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS 21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS 22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS 23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS 24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS 25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
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FILE 'HOME' ENTERED AT 09:03:09 ON 18 APR 2006

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FULL ESTIMATED COST 0.21 0.21

FILE 'CAPLUS' ENTERED AT 09:03:17 ON 18 APR 2006
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FILE LAST UPDATED: 17 Apr 2006 (20060417/ED)

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=> s cofilin
777 COFILIN
232 COFILINS
L1 814 COFILIN
(COFILIN OR COFILINS)

=> s inhibit?
L2 1822517 INHIBIT?

=> s l1 (L) l2
L3 221 L1 (L) L2

=> s hepatocar? or mesenchy? or nuroectoder? or (ewing?)
7077 HEPATOCAR?
15151 MESENCHY?
0 NUROECTODER?
1659 EWING?

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L4       23829 HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)

=> s l3 and l4
L5           1 L3 AND L4

=> d ibib

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2002:977858  CAPLUS
DOCUMENT NUMBER:          138:52333
TITLE:                    Pharmaceutical composition for diagnosis, prevention
                          or treatment of a tumorous state, comprising a
                          modulator of the actin polymerization state
INVENTOR(S):              Auclair, Christian; Amsellem, Valerie; Hervy, Martial;
                          Subra, Frederic
PATENT ASSIGNEE(S):       Bioalliance Pharma, Fr.; Ecole Normale Superieure De
                          Cachan; Institut Gustave Roussy-IGR; Centre National
                          de la Recherche Scientifique CNRS
SOURCE:                   PCT Int. Appl., 68 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2002102846         A2    20021227    WO 2002-FR2106           20020618
     WO 2002102846         A3    20040422
     WO 2002102846         B1    20040603
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
             GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
             GN, GQ, GW, ML, MR, NE, SN, TD, TG
     FR 2825928            A1    20021220    FR 2001-7976             20010618
     FR 2825928            B1    20040402
     CA 2450845            AA    20021227    CA 2002-2450845          20020618
     EP 1432732            A2    20040630    EP 2002-745538           20020618
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2005504521         T2    20050217    JP 2003-506318           20020618
     US 2004191230         A1    20040930    US 2003-740266           20031218
PRIORITY APPLN. INFO.:                         FR 2001-7976          A  20010618
                                               WO 2002-FR2106        W  20020618


=> s actin
         49687 ACTIN
         30340 ACTINS
L6       52687 ACTIN
                (ACTIN OR ACTINS)

=> s stabil?
L7     1026058 STABIL?

=> s l6 (l) l7
L8        2489 L6 (L) L7

=> d his
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      (FILE 'HOME' ENTERED AT 09:03:09 ON 18 APR 2006)

      FILE 'CAPLUS' ENTERED AT 09:03:17 ON 18 APR 2006
L1           814 S COFILIN
L2       1822517 S INHIBIT?
L3           221 S L1 (L) L2
L4         23829 S HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)
L5             1 S L3 AND L4
L6         52687 S ACTIN
L7       1026058 S STABIL?
L8          2489 S L6 (L) L7

=> s l8 and l4
L9           19 L8 AND L4

=> s l9 not py>2002
       3759065 PY>2002
L10           8 L9 NOT PY>2002

=> s l9 not py>2001
       4742175 PY>2001
L11           8 L9 NOT PY>2001

=> d ibib 1-8

L11  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2002:88952  CAPLUS
DOCUMENT NUMBER:          136:242165
TITLE:                    TGFβ is required for the formation of
                          capillary-like structures in three-dimensional
                          cocultures of 10T1/2 and endothelial cells
AUTHOR(S):                Darland, D. C.; D'Amore, P. A.
CORPORATE SOURCE:         The Schepens Eye Research Institute and the Department
                          of Ophthalmology, Harvard Medical School, Boston, MA,
                          02114, USA
SOURCE:                   Angiogenesis (2001), 4(1), 11-20
                          CODEN: AGIOFT; ISSN: 0969-6970
PUBLISHER:                Kluwer Academic Publishers
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          51    THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11  ANSWER 2 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2001:7412  CAPLUS
DOCUMENT NUMBER:          134:264229
TITLE:                    Integrin α3β1 engagement disrupts
                          intercellular adhesion
AUTHOR(S):                Kawano, Kenji; Kantak, Seema S.; Murai, Mutsuhiko;
                          Yao, Chung-Chen; Kramer, Randall H.
CORPORATE SOURCE:         Department of Stomatology, University of California at
                          San Francisco, San Francisco, CA, 94143-0512, USA
SOURCE:                   Experimental Cell Research (2001), 262(2), 180-196
                          CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER:                Academic Press
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          66    THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11  ANSWER 3 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2000:336418  CAPLUS
DOCUMENT NUMBER:          133:87270
TITLE:                    The tetraspan molecule CD151, a novel constituent of
```

hemidesmosomes, associates with the integrin α6β4 and may regulate the spatial organization of hemidesmosomes

AUTHOR(S): Sterk, Lotus M. Th.; Geuijen, Cecile A. W.; Oomen, Lauran C. J. M.; Calafat, Jero; Janssen, Hans; Sonnenberg, Arnoud

CORPORATE SOURCE: Division of Cell Biology, The Netherlands Cancer Institute, Amsterdam, 1066 CX, Neth.

SOURCE: Journal of Cell Biology (2000), 149(4), 969-982
CODEN: JCLBA3; ISSN: 0021-9525

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:517212 CAPLUS

DOCUMENT NUMBER: 129:170359

TITLE: Expression of human bone morphogenic protein 7 in primary rabbit periosteal cells. Potential utility in gene therapy for osteochondral repair

AUTHOR(S): Mason, J. M.; Grande, D. A.; Barcia, M.; Grant, R.; Pergolizzi, R. G.; Breitbart, A. S.

CORPORATE SOURCE: Viral Vector Lab., Dep. Res., North Shore Univ. Hosp.-New York Univ. Sch. Med., Manhasset, NY, 11030, USA

SOURCE: Gene Therapy (1998), 5(8), 1098-1104
CODEN: GETHEC; ISSN: 0969-7128

PUBLISHER: Stockton Press

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:269919 CAPLUS

DOCUMENT NUMBER: 126:260361

TITLE: Modulation of LDL receptor mRNA stability by phorbol esters in human liver cell culture models

AUTHOR(S): Wilson, G. M.; Roberts, E. A.; Deeley, R. G.

CORPORATE SOURCE: Department of Biochemistry and Cancer Research Laboratories, Queen's University, Kingston, ON, Can.

SOURCE: Journal of Lipid Research (1997), 38(3), 437-446
CODEN: JLPRAW; ISSN: 0022-2275

PUBLISHER: Lipid Research, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:145098 CAPLUS

DOCUMENT NUMBER: 116:145098

TITLE: Gene regulatory factors of the sea urchin embryo. I. Purification by affinity chromatography and cloning of P3A2, a novel DNA-binding protein

AUTHOR(S): Calzone, Frank J.; Hoeoeg, Christer; Teplow, David B.; Cutting, Ann E.; Zeller, Robert W.; Britten, Roy J.; Davidson, Eric H.

CORPORATE SOURCE: Div. Biol., California Inst. Technol., Pasadena, CA, 91125, USA

SOURCE: Development (Cambridge, United Kingdom) (1991), 112(1), 335-50
CODEN: DEVPED; ISSN: 0950-1991

DOCUMENT TYPE: Journal
LANGUAGE: English

L11 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:595544 CAPLUS
DOCUMENT NUMBER: 107:195544
TITLE: Developmental and tissue-specific regulation of β-tubulin gene expression in the embryo of the sea urchin Strongylocentrotus purpuratus
AUTHOR(S): Harlow, Patricia; Nemer, Martin
CORPORATE SOURCE: Inst. Cancer Res., Fox Chase Cancer Cent., Philadelphia, PA, 19111, USA
SOURCE: Genes & Development (1987), 1(2), 147-60
CODEN: GEDEEP; ISSN: 0890-9369
DOCUMENT TYPE: Journal
LANGUAGE: English

L11 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:140906 CAPLUS
DOCUMENT NUMBER: 98:140906
TITLE: A yellow crescent cytoskeletal domain in ascidian eggs and its role in early development
AUTHOR(S): Jeffery, William R.; Meier, Stephen
CORPORATE SOURCE: Dep. Zool., Univ. Texas, Austin, TX, 78712, USA
SOURCE: Developmental Biology (Orlando, FL, United States) (1983), 96(1), 125-43
CODEN: DEBIAO; ISSN: 0012-1606
DOCUMENT TYPE: Journal
LANGUAGE: English

=> d kwic 3

L11 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AB . . . and certain integrins to form large complexes at the cell surface. CD151 is expressed by a variety of epithelia and mesenchymal cells. We demonstrate here that in human skin CD151 is codistributed with α3β1 and α6β4 at the basolateral surface of. . . cell surface in association with patches of laminin-5. Focal adhesions are present at the periphery of these clusters, connected with actin filaments, and they contain both CD151 and α3β1. Transient transfection studies of PA-JEB cells with β4 revealed that the integrin. . . recruitment into hemidesmosomes is regulated by the integrin α6β4. We suggest that CD151 plays a role in the formation and stability of hemidesmosomes by providing a framework for the spatial organization of the different hemidesmosomal components.

=> s dolastatin or jasplakinolide
390 DOLASTATIN
59 DOLASTATINS
404 DOLASTATIN
(DOLASTATIN OR DOLASTATINS)
251 JASPLAKINOLIDE
1 JASPLAKINOLIDES
252 JASPLAKINOLIDE
(JASPLAKINOLIDE OR JASPLAKINOLIDES)
L12 652 DOLASTATIN OR JASPLAKINOLIDE

=> d his

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FILE 'CAPLUS' ENTERED AT 09:03:17 ON 18 APR 2006

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L1          814 S COFILIN
L2      1822517 S INHIBIT?
L3          221 S L1 (L) L2
L4        23829 S HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)
L5            1 S L3 AND L4
L6        52687 S ACTIN
L7      1026058 S STABIL?
L8         2489 S L6 (L) L7
L9           19 S L8 AND L4
L10           8 S L9 NOT PY>2002
L11           8 S L9 NOT PY>2001
L12         652 S DOLASTATIN OR JASPLAKINOLIDE

=> s l12 and l4
L13           8 L12 AND L4

=> s l13 not py>2001
       4742175 PY>2001
L14           0 L13 NOT PY>2001

=> s l13 not py>2002
       3759065 PY>2002
L15           0 L13 NOT PY>2002

=> d l13 ibib 1-8

L13  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:13464  CAPLUS
DOCUMENT NUMBER:          144:101073
TITLE:                    therapeutic uses of kinase inhibitors, and
                          compositions thereof
INVENTOR(S):              Caligiuri, Maureen G.; Kley, Nikolai A.; Murthi,
                          Krishna K.
PATENT ASSIGNEE(S):       GPC Biotech, Inc., USA
SOURCE:                   PCT Int. Appl., 201 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2006002119         A2    20060105    WO 2005-US21843         20050617
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM,
             KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG,
             KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                          US 2004-580868P     P  20040618
OTHER SOURCE(S):          MARPAT 144:101073

L13  ANSWER 2 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:1290072  CAPLUS
DOCUMENT NUMBER:          144:46998
TITLE:                    The X-ray crystal structure of BRCA1 tandem BRCT
                          repeat and BACH1 phosphopeptide complex and methods
                          and compositions for antitumor drug design
```

INVENTOR(S): Yaffe, Michael B.; Clapperton, Julie A.; Manke, Isaac A.; Lowery, Drew M.; Ho, Timmy; Haire, Lesley F.; Smerdon, Stephen J.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 360 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005115454	A2	20051208	WO 2005-US15981	20050509

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-569131P P 20040507

L13 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409543 CAPLUS
DOCUMENT NUMBER: 142:457053
TITLE: Human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy
INVENTOR(S): Lacasse, Eric; McManus, Daniel
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042558	A1	20050512	WO 2004-CA1902	20041029

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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US 2005148535	A1	20050707	US 2004-975974	20041028

PRIORITY APPLN. INFO.: US 2003-516192P P 20031030

L13 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409357 CAPLUS
DOCUMENT NUMBER: 142:457052
TITLE: Sequences of antisense IAP (inhibitor of apoptosis

protein) oligomers and their use for treatment of proliferative diseases with a chemotherapeutic agent

INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042030	A1	20050512	WO 2004-CA1900	20041029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005119217	A1	20050602	US 2004-975790	20041028

PRIORITY APPLN. INFO.: US 2003-516263P P 20031030
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:283298 CAPLUS
DOCUMENT NUMBER: 142:349042
TITLE: Combinations of chlorpromazine compounds and antiproliferative drugs for the treatment of neoplasms

INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen; Keith, Curtis
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916
WO 2005027842	A3	20051222		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2003-504310P P 20030918
OTHER SOURCE(S): MARPAT 142:349042

L13 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:248055 CAPLUS

DOCUMENT NUMBER: 142:352644
TITLE: RhoA/ROCK Signaling Regulates Sox9 Expression and Actin Organization during Chondrogenesis
AUTHOR(S): Woods, Anita; Wang, Guoyan; Beier, Frank
CORPORATE SOURCE: Canadian Institutes of Health Research Group in Skeletal Development and Remodeling, Department of Physiology and Pharmacology, University of Western Ontario, London, ON, N6A 5C1, Can.
SOURCE: Journal of Biological Chemistry (2005), 280(12), 11626-11634
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:816528 CAPLUS
DOCUMENT NUMBER: 140:12638
TITLE: Two CD95 tumor classes with different sensitivities to antitumor drugs
AUTHOR(S): Algeciras-Schimnich, Alicia; Pietras, Eric M.; Barnhart, Bryan C.; Legembre, Patrick; Vijayan, Shrijay; Holbeck, Susan L.; Peter, Marcus E.
CORPORATE SOURCE: The Ben May Institute for Cancer Research, University of Chicago, Chicago, IL, 60637, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(20), 11445-11450
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:924095 CAPLUS
DOCUMENT NUMBER: 136:31647
TITLE: Toxicity typing using mesenchymal stem cells
INVENTOR(S): Snodgrass, H. Ralph
PATENT ASSIGNEE(S): Vistagen, Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096865	A1	20011220	WO 2001-US19048	20010614
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2412769	AA	20011220	CA 2001-2412769	20010614
US 2002045179	A1	20020418	US 2001-881475	20010614
EP 1290443	A1	20030312	EP 2001-946335	20010614

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        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
    JP 2004503255        T2    20040205    JP 2002-510943          20010614
PRIORITY APPLN. INFO.:                     US 2000-211608P     P   20000614
                                           WO 2001-US19048     W   20010614
REFERENCE COUNT:          7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> file pctfull
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      51.50      51.71

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)            SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                      -0.75      -0.75

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MOST RECENT UPDATE WEEK:        200614        <200614/EW>
FILE COVERS 1978 TO DATE

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>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
    SEE
    http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE
    (last updated April 10, 2006) <<<

=> s dolastatin or jasplakinolide
           459 DOLASTATIN
            70 DOLASTATINS
           477 DOLASTATIN
                 (DOLASTATIN OR DOLASTATINS)
           171 JASPLAKINOLIDE
             1 JASPLAKINOLIDES
           171 JASPLAKINOLIDE
                 (JASPLAKINOLIDE OR JASPLAKINOLIDES)
L16        643 DOLASTATIN OR JASPLAKINOLIDE

=> s hepatocar? or mesenchy? or nuroectoder? or (ewing?)
           770 HEPATOCAR?
          5688 MESENCHY?
             0 NUROECTODER?
          3185 EWING?
L17       8782 HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)

=> s l17 and l16
L18        243 L17 AND L16

=> s l18 not py>2001
        488865 PY>2001
L19         16 L18 NOT PY>2001

=> s l16/clm
            60 DOLASTATIN/CLM
             7 JASPLAKINOLIDE/CLM
L20         67 (DOLASTATIN/CLM OR JASPLAKINOLIDE/CLM)

=> s l20 and l19
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L21          0 L20 AND L19

=> s l19 not py>2000
        587352 PY>2000
L22          8 L19 NOT PY>2000

=> d ibib 1-8

L22    ANSWER 1 OF 8      PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:         2000071135 PCTFULL  ED 20020515
TITLE (ENGLISH):          ANTI-TUMOR COMPRISING BOROPROLINE COMPOUNDS
TITLE (FRENCH):           AGENTS ANTI-TUMORALES CONTENANT DES COMPOSES DE
                          BOROPROLINE
INVENTOR(S):              WALLNER, Barbara, P.;
                          MILLER, Glenn
PATENT ASSIGNEE(S):       POINT THERAPEUTICS, INC.
LANGUAGE OF PUBL.:        English
DOCUMENT TYPE:            Patent
PATENT INFORMATION:

                          NUMBER              KIND     DATE
                          ---------------------------------
                          WO 2000071135         A1 20001130

DESIGNATED STATES
       W:                 AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ
                          DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
                          JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
                          MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
                          TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ
                          TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK
                          ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM
                          GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:        WO 2000-US14505       A  20000525
PRIORITY INFO.:           US 1999-60/135,861       19990525

L22    ANSWER 2 OF 8      PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:         2000067802 PCTFULL  ED 20020515
TITLE (ENGLISH):          FATTY ACID-N-SUBSTITUTED INDOL-3-GLYOXYL-AMIDE
                          COMPOSITIONS AND USES THEREOF
TITLE (FRENCH):           COMPOSITIONS D'ACIDES GRAS -N-SUBSTITUTED
                          INDOL-3-GLYOXYL-AMIDE ET LEUR UTILISATION
INVENTOR(S):              BRADLEY, Matthews, O.;
                          SWINDELL, Charles, S.;
                          ANTHONY, Forrest;
                          WEBB, Nigel, L.;
                          FISHER, Mark
PATENT ASSIGNEE(S):       PROTARGA, INC.
LANGUAGE OF PUBL.:        English
DOCUMENT TYPE:            Patent
PATENT INFORMATION:

                          NUMBER              KIND     DATE
                          ---------------------------------
                          WO 2000067802         A1 20001116

DESIGNATED STATES
       W:                 AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ
                          DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
                          JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
                          MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
                          TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG
                          ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI
                          FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN
                          GW ML MR NE SN TD TG
APPLICATION INFO.:        WO 2000-US12752       A  20000510
PRIORITY INFO.:           US 1999-60/133,292       19990510

L22    ANSWER 3 OF 8      PCTFULL   COPYRIGHT 2006 Univentio on STN
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ACCESSION NUMBER: 2000064946 PCTFULL ED 20020515
TITLE (ENGLISH): COMPOSITIONS AND METHODS FOR CANCER TREATMENT BY SELECTIVELY INHIBITING VEGF
TITLE (FRENCH): COMPOSITIONS ET PROCEDES DE TRAITEMENT DU CANCER PAR INHIBITION SELECTIVE DE VEGF
INVENTOR(S): THORPE, Philip, E.;
BREKKEN, Rolf, A.
PATENT ASSIGNEE(S): BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000064946	A2	20001102

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2000-US11367 A 20000428
PRIORITY INFO.: US 1999-60/131,432 19990428

L22 ANSWER 4 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2000050016 PCTFULL ED 20020515
TITLE (ENGLISH): COMPOSITIONS AND METHODS FOR IMPROVING INTEGRITY OF COMPROMISED BODY PASSAGEWAYS AND CAVITIES
TITLE (FRENCH): COMPOSITIONS ET METHODES POUR L'AMELIORATION DE L'INTEGRITE DE CAVITES ET DE PASSAGES CORPORELS AFFAIBLIS
INVENTOR(S): SIGNORE, Pierre, E.;
MACHAN, Lindsay, S.
PATENT ASSIGNEE(S): ANGIOTECH PHARMACEUTICALS, INC.;
SIGNORE, Pierre, E.;
MACHAN, Lindsay, S.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000050016	A2	20000831

DESIGNATED STATES
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2000-CA175 A 20000223
PRIORITY INFO.: US 1999-60/121,424 19990223

L22 ANSWER 5 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999062510 PCTFULL ED 20020515
TITLE (ENGLISH): COMPOSITIONS COMPRISING ANTI-MICROTUBULE AGENTS FOR TREATING OR PREVENTING INFLAMMATORY DISEASES
TITLE (FRENCH): COMPOSITIONS RENFERMANT DES AGENTS ANTI-MICROTUBULES POUR LE TRAITEMENT OU LA PREVENTION DE MALADIES INFLAMMATOIRES
INVENTOR(S): HUNTER, William, L.
PATENT ASSIGNEE(S): ANGIOTECH PHARMACEUTICALS, INC.;

HUNTER, William, L.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9962510	A2	19991209

DESIGNATED STATES
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 1999-CA464 A 19990601
PRIORITY INFO.: US 1998-09/088,546 19980601

L22 ANSWER 6 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999055343 PCTFULL ED 20020515
TITLE (ENGLISH): CNRE BINDING FACTORS AND USES THEREOF
TITLE (FRENCH): FACTEURS DE LIAISON CNRE ET UTILISATIONS CORRESPONDANTES
INVENTOR(S): CHEN, Yuqing, E.;
HORIUCHI, Masatsugu;
DZAU, Victor, J.;
TAMURA, Koichi
PATENT ASSIGNEE(S): THE BRIGHAM AND WOMEN'S HOSPITAL, INC.;
CHEN, Yuqing, E.;
HORIUCHI, Masatsugu;
DZAU, Victor, J.;
TAMURA, Koichi
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9955343	A1	19991104

DESIGNATED STATES
W: CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1999-US8502 A 19990423
PRIORITY INFO.: US 1998-60/082,997 19980424

L22 ANSWER 7 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999004817 PCTFULL ED 20020515
TITLE (ENGLISH): CHEMOTHERAPY SYNERGISTIC AGENT
TITLE (FRENCH): AGENT SYNERGIQUE POUR CHIMIOTHERAPIE
INVENTOR(S): WINKELMAN, James, W.;
BRIDGES, Kenneth, R.
PATENT ASSIGNEE(S): BRIGHAM & WOMEN'S HOSPITAL, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9904817	A1	19990204

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-US15052 A 19980722
PRIORITY INFO.: US 1997-60/053,696 19970725
US 1997-60/054,148 19970725

L22 ANSWER 8 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 1998035554 PCTFULL ED 20020514
TITLE (ENGLISH): COMBINED TUMOR SUPPRESSOR GENE THERAPY AND CHEMOTHERAPY IN THE TREATMENT OF NEOPLASMS
TITLE (FRENCH): COMBINAISON THERAPIE GENIQUE SUPPRESSIVE DE TUMEURS - CHIMIOTHERAPIE UTILISEE DANS LE TRAITEMENT DE NEOPLASMES
INVENTOR(S): NIELSEN, Loretta;
HOROWITZ, Jo, Ann;
MANEVAL, Daniel, C.;
DEMERS, G., William;
RYBAK, Mary, Ellen;
RESNICK, Gene
PATENT ASSIGNEE(S): CANJI, INC.;
NIELSEN, Loretta;
HOROWITZ, Jo, Ann;
MANEVAL, Daniel, C.;
DEMERS, G., William;
RYBAK, Mary, Ellen;
RESNICK, Gene
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9835554	A2	19980820

DESIGNATED STATES
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1998-US3514	A	19980217
PRIORITY INFO.:	US 1997-8/801,285		19970218
	US 1997-8/801,681		19970218
	US 1997-8/801,755		19970218
	US 1997-8/801,765		19970218
	US 1997-60/038,065		19970218
	US 1997-60/047,834		19970528

=> d kwic 5, 7

L22 ANSWER 5 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . subtilisin, 1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol, flavanol, rotenone, griseofulvin, vinca alkaloids, including
vinblastine and vincristine, maytansinoids and ansamitocins, rhizoxin, phornopsin A,
ustiloxins, dolastatin 10, dolastatin 15,
halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam. betaine. taurine, isethionate, HO-221, adociasulfate-2,
estramustine, monoclonal anti-idiotypic antibodies, microtubule assembly promoting
protein (taxol-like protein, TALP),. . .
. . .
phomopsin A (Hamel, Med. Res. Rev. 16(2): 207-23) 1, 1996), ustiloxins
(Hamel, Med Res. Rev. 16(2): 207-23) 1, 1996), dolastatin I 0
(Hamel, Med. Res. Rev.

16(2): 207-23) 1, 1996). dolastatin 15 (Hamel. Med Res. Rev.

16(2): 207-23) 1, 1996),
halichondrins and halistatins (Hamel, Med. Res. Rev. 16(2): 207-231, 1996),
spongistatins (Hamel,. . .
. . .
subtilisin,
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maytansinoids and ansamitocins, rhizoxin. phomopsin A. ustiloxins,
dolastatin 10,
dolastatin 15, halichondrins and halistatins, spongistatins.
cryptophycins, rhazinilam,
betaine, taurine, isethionate. HO-221, adociasulfate-2, estramustine.
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein
(taxol-like. . .
. . .
subtilisin,
1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxvestradiol, flavanol,
rotenone, griseofulvin, vinca alkaloids, including vinblastine and vincristine,
maytansinoids and ansamitocins. rhizoxin, phomopsin A, ustiloxins,
dolastatin I 0,
dolastatin 15, halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam,
betaine, taurine, isethionate, HO-221, adociasulfate-2, estrainustine.
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein
(taxol-like. . .
. . .
subtilisin,
1069C85. steganacin. combretastatin. curacin, estradiol,
2-methoxyestradiol. flavanol,
rotenone, griseofulvin, vinca alkaloids. including vinblastine and vincristine,
maytansinoids and ansamitocins, rhizoxin. phornopsin A, ustiloxins.
dolastatin 10,
dolastatin 15. halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilarn,
betaine, taurine, isethionate, HO-221, adociasulfate-2, estramustine,
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein
(taxol-like. . .
. . .
subtilisin,
1069C85. steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol, flavanol,
rotenone. griseofulvin, vinca alkaloids, including vinblastine and vincristine,
maytansinoids and ansamitocins, rhizoxin, phomopsin A, ustiloxins,
dolastatin 10.

dolastatin 15, halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam,
betaine, taurine, isethionate, HO-221, adociasulfate-2, estramustine,
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein
(taxol-like. . .
. . .
subtilisin. 1069C85, steganacin,
combretastatin, curacin, estradiol, 2-methoxyestradiol, flavanol,
rotenone, griseofulvin,

vinca alkaloids. including vinblastine and vincristine, maytansinoids and ansamitocins,
rhizoxin, phomopsin A. ustiloxins, dolastatin 10.
dolastatin 15, halichondrins and
halistatins, spongistatins, cryptophycins, rhazinilam, betaine, taurine.
isethionate, HO-
221, adociasulfate-2, estramustine. monoclonal anti-idiotypic
antibodies. microtubule
assembly promoting protein (taxol-like protein,. . .

maytansinoids and ansainitocins, rhizoxin. phomopsin A, ustiloxins,
dolastatin I 0,
dolastatin 15, halichondrins and halistatins, spongistatins,
cryptophycins. rhazinilam,
betaine, taurine, isethionate, HO-22 1, adociasulfate-2, estraniustine,
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein. . .
. .
subtilisin,
1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol. flavanol,
rotenone, griseofulvin. vinca alkaloids. including vinblastine and
vincristine,
maytansinoids and ansamitocins, rhizoxin, phomopsin A, ustiloxins.
dolastatin 10.

dolastatin 15, halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam,
betaine. taurine. isethionate, HO-221, adociasulfate-2, estramustine,
microtubule
assembly promoting protein (taxol-like protein, TALP), cell swelling. .
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. .
subtilisin,
1069C85. steganacin, combretastatin, curacin. estradiol,
2-methoxyestradiol. flavanol,
rotenone, griseofulvin, vinca alkaloids, including vinblastine and
vincristine,
maytansinoids and ansamitocins, rhizoxin, phomopsin A, ustiloxins,
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dolastatin 15, halichondrins and halistatins, sponcristatins,
cryptophycins, rhazinilam,
betaine, taurine, isethionate, HO-221, adociasulfate-2, estramustine,
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein
(taxol-like. . .
. .
subtilisin,
1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol, flavanol,
rotenone, griseofulvin. vinca alkaloids, including vinblastine and
vincristine,
maytansinoids and ansamitocins, rhizoxin, phomopsin A. ustiloxins,
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dolastatin 15, halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam,
betaine, taurine, isethionate, HO-221, adociasulfate-2, estramustine,
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein
(taxol-like. . .
. .
subtilisin,
1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol, flavanol,
rotenone, griseofulvin. vinca alkaloids, including vinblastine and

vincristine,
maytansinoids and ansamitocins, rhizoxin, phornopsin A. ustiloxins,
dolastatin 10,
dolastatin 15, halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam,
betaine, taurine, isethionate, HO-221, adociasulfate-2, estramustine,
microtubule
assembly promoting protein (taxol-like protein, TALP), cell swelling. .
.
. . .
subtilisin, 1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol, flavanol, rotenone, griseofulvin, vinca alkaloids,
including
vinblastine and vincristine; maytansinoids and ansamitocins, rhizoxin,
phomopsin A,
ustiloxins, dolastatin 10, dolastatin 15,
halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam, betaine, taurine, isethionate, HO-221,
adociasulfate-2,
estramustine, monoclonal anti-idiotypic antibodies, microtubule assembly
promoting
protein (taxol-like protein, TALP),. . .
. . .
subtilisin, 1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol, flavanol, rotenone, griseofulvin, vinca alkaloids,
including
vinblastine and vincristine. maytansinoids and ansamitocins, rhizoxin,
phomopsin A,
ustiloxins, dolastatin 10, dolastatin 15,
halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam, betaine, taurine, isethionate. HO-221,
adociasulfate
estramustine, monoclonal anti-idiotypic antibodies, microtubule assembly
promoting
protein (taxol-like protein.. . .
. . .
subtilisin, 1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol, flavanol, rotenone, griseofulvin, vinca alkaloids,
including
vinblastine and vincristine, maytansinoids and ansamitocins, rhizoxin,
phomopsin A,
ustiloxins, dolastatin 10, dolastatin 15,
halichondrins and halistatins. spongistatins.
. . .
endpoints: (1) inhibition of
the white blood cell response (macrophages, neutrophils and T cells)
which initiates the
inflammatory cascade; (2) inhibition of mesenchyrnal cell
(fibroblasts, synoviocytes,
etc.) hyperproliferation that leads to the development of fibrosis and
loss of organ
function; (3) inhibition of matrix metalloproteinase. . .

L22 ANSWER 7 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . 91)

lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous
cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal
cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal
cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcorna and
osteosarcoma; skin

cancer, including melanoma, Kaposi's sarcoma, basal. . .
. . .
peptides; insulin-like
growth factor-I receptor inhibitor; interferon agonists; interferons;
interleukins; iobenguane;
I 0 iododoxorubicin; ipomeanol, 4-; irinotecan; iroplact; irsogladine;
isobengazole;
isohomohalicondrin B; itasetron; jasplakinolide; kahalalide F;
larnellarin-N triacetate;
lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin;
letrozole; leukemia
inhibiting factor; leukocyte alpha interferon; leuprolide + estrogen +
progesterone;
leuprorelin;. . .

CLMEN. . . and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous
cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal
cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal
cancer; sarcomas, including
leiornyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and
osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basocellular. . .
. . .
and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squarnous
cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal
cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal
cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and
osteosarcoma; skin
- 24 -
cancer, including melanoma, Kaposi's. . .
. . .
and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous
cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal
cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer'; rectal
cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and
osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma; basocellular. . .

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TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 8	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 13	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 14	DEC 18	CA/CAplus patent kind codes updated
NEWS 15	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 17	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 23	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 24	JAN 29	PHAR reloaded with new search and display fields
NEWS 25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 26	FEB 13	CASREACT coverage to be extended
NEWS 27	Feb 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 28	Feb 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 29	Feb 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 30	Feb 26	MEDLINE reloaded with enhancements
NEWS 31	Feb 26	EMBASE enhanced with Clinical Trial Number field
NEWS 32	Feb 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 33	Feb 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 34	Feb 26	CAS Registry Number crossover limit increased from 10,000

to 300,000 in multiple databases

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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=> s ESP-2 or HED-2 or Zyxin or Zyxin-2
        511000 ESP
           263 ESPS
        511131 ESP
                  (ESP OR ESPS)
       9071127 2
           958 ESP-2
                  (ESP(W)2)
           397 HED
            35 HEDS
           428 HED
                  (HED OR HEDS)
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        9071127 2
              5 HED-2
                  (HED(W)2)
            249 ZYXIN
             28 ZYXINS
            254 ZYXIN
                  (ZYXIN OR ZYXINS)
            249 ZYXIN
             28 ZYXINS
            254 ZYXIN
                  (ZYXIN OR ZYXINS)
        9071127 2
              6 ZYXIN-2
                  (ZYXIN(W)2)
L1        1213 ESP-2 OR HED-2 OR ZYXIN OR ZYXIN-2

=> s cancer? or tumor? or neoplas?
         323384 CANCER?
         460516 TUMOR?
         483669 NEOPLAS?
L2       763127 CANCER? OR TUMOR? OR NEOPLAS?

=> s l1 (L) l2
L3           73 L1 (L) L2

=> s therap? or treat? or inhibit? or suppres?
         509077 THERAP?
        3519011 TREAT?
        1906473 INHIBIT?
         411937 SUPPRES?
L4      5345131 THERAP? OR TREAT? OR INHIBIT? OR SUPPRES?
 75% OF LIMIT FOR TOTAL ANSWERS REACHED

=> s l4 and l3
L5           55 L4 AND L3

=> s l5 not py>2000
        6894468 PY>2000
L6           14 L5 NOT PY>2000

=> d ibib abs 1-7

L6   ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2000:738475  CAPLUS
DOCUMENT NUMBER:          134:220517
TITLE:                    Alterations in the gene expression profile of MCF-7
                          breast tumor cells in response to c-Jun
AUTHOR(S):                Rinehart-Kim, Janet; Johnston, Melissa; Birrer,
                          Michael; Bos, Timothy
CORPORATE SOURCE:         Department of Microbiology and Molecular Cell Biology,
                          Eastern Virginia Medical School, Norfolk, VA, USA
SOURCE:                   International Journal of Cancer (2000), 88(2), 180-190
                          CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER:                Wiley-Liss, Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   MCF7 breast tumor cells overexpressing human c-Jun exhibit a transformed
     phenotype characterized not only by increased tumorigenicity but also by
     enhanced motility and invasion.  The cellular phenotypic response to c-Jun
     overexpression is likely due, at least in part, to altered patterns of
     gene expression.  In order to begin to understand the complexities by
     which elevated production of c-Jun alters the state of the cell, the authors
     have profiled the expression of 588 different genes by comparative
     hybridization.  By using this approach, the authors have identified a
     total of 21 upregulated or downregulated gene targets responsive to c-Jun
```

overexpression. Interestingly, 8 of these genes have been previously found associated with c-Jun or AP-I activity and therefore provide internal validation for this approach to target gene discovery. The remaining 13 genes represent potential new c-Jun regulated target genes. Genomic sequence information was available for 15 of the 21 genes identified in this screen. Anal. of these genomic sequences revealed the presence of AP-I or AP-I-like sequences in 12 of the 15 genes examined Consistent with a direct mechanism of target regulation by c-Jun, gel shift anal. of selected AP-I-containing promoter regions revealed elevated and specific binding by proteins present in nuclear exts. of c-Jun expressing MCF7 cells.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:734436 CAPLUS
DOCUMENT NUMBER: 134:14198
TITLE: Differential display analysis of fiber-induced carcinogenesis in rat: clue for involvement of integrin-mediated signal transduction
AUTHOR(S): Sandhu, H.; Olbruck, H.; Abel, J.; Unfried, K.
CORPORATE SOURCE: Department of Experimental Toxicology, Medical Institute of Environmental Hygiene at the Heinrich Heine University, Dusseldorf, 40225, Germany
SOURCE: Inhalation Toxicology (2000), 12(Suppl. 3), 337-343
CODEN: INHTE5; ISSN: 0895-8378
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study, mRNA expression patterns during mesothelioma carcinogenesis in the peritoneal cavity were investigated. To this purpose, the mRNA expression patterns of fiber-induced mesothelioma and of fiber-treated tissues were compared to untreated tissues, resp. Suppression subtractive hybridization (SSH) and an array hybridization assay were used to perform differential display analyses. Genes found to be expressed differentially mainly represent proteins of signal transduction pathways and regulatory proteins of the cell cycle. The genes for components of the AP-1 transcription factor, c-jun, c-fos, and fra-1 (fos-related antigen-1) are upregulated in nontumorous tissue treated with asbestos. These data confirm in vivo the involvement of AP-1 expression as response to fiber treatment. In addition, osteopontin, zyxin, and integrin-linked kinase were upregulated in tumors and in treated tissues. These genes code for proteins involved in the signal transduction from the extracellular matrix to the nucleus. Using integrin-specific inhibitors, the apoptotic effects of crocidolite fibers could be suppressed significantly. From these results the authors hypothesize that direct effects of the fibers on the target tissue are mediated by interaction of the fibers with the extracellular matrix mols.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:727041 CAPLUS
DOCUMENT NUMBER: 134:81
TITLE: Preparation of novel specific aminopeptidase inhibitors with a cyclic imide skeleton
AUTHOR(S): Takahashi, Hiroyasu; Komoda, Masato; Katsuta, Hiroki; Hashimoto, Yuichi
CORPORATE SOURCE: Institute of Molecular and Cellular Bioscience, University of Tokyo, Tokyo, 113-0032, Japan
SOURCE: Yakugaku Zasshi (2000), 120(10), 909-922
CODEN: YKKZAJ; ISSN: 0031-6903
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review with 25 refs. The studies on both structure-activity relationship study and identification of the target enzyme of novel nonpeptide aminopeptidase inhibitors with cyclic imide skeleton are reviewed. Some N-phenylphthalimide or N-phenylhomophthalimide derivative showed potent protease inhibitory activity in an assay system using human acute lymphoblastic leukemia cells, Molt-4, with alanine-4-methylcoumaryl-7-amide (ala-AMC) as a substrate. Esp ., 2-(2,6-diethylphenyl)-1,2,3,4-tetrahydroisoquinoline-1,3-dione (PIQ-22) (3) was found to be the most potent inhibitor and further it showed potent tumor-cell invasion inhibitory activity that is more effective than potent peptide aminopeptidase inhibitors such as bestatin (1) or actinonin (2). For the further investigation of this novel protease inhibitory activity, we have carried out the structural development of PIQ-22 (3) and it is assumed that tautomerism of imidobenzoylketone in cyclic imide structure may be related to the inhibitory activity. The requirement for the activity of electron donating groups such as NH2 or OH to the condensed Ph ring in phthalimide inhibitors also supports this possibility. The target aminopeptidase of PIQ-22 was identified as puromycin-sensitive aminopeptidase (PSA), by N-terminal amino acid sequencing, and by comparison with chromatog. behavior and substrate-selectivity, and so on. Lineweaver-Burk plot showed that PSA is inhibited by PIQ-22 (3) in a noncompetitive manner while puromycin (83) and bestatin (1) inhibit PSA competitively.

L6 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:393023 CAPLUS

DOCUMENT NUMBER: 133:117982

TITLE: Zyxin, a regulator of actin filament assembly, targets the mitotic apparatus by interacting with h-warts/LATS1 tumor suppressor

AUTHOR(S): Hirota, Toru; Morisaki, Tetsuro; Nishiyama, Yasuyuki; Marumoto, Tomotoshi; Tada, Kenji; Hara, Toshihiro; Masuko, Norio; Inagaki, Masaki; Hatakeyama, Katsuyoshi; Saya, Hideyuki

CORPORATE SOURCE: Department of Tumor Genetics and Biology, Kumamoto University School of Medicine, Kumamoto, 860-0811, Japan

SOURCE: Journal of Cell Biology (2000), 149(5), 1073-1086
CODEN: JCLBA3; ISSN: 0021-9525

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The mitotic apparatus plays a pivotal role in dividing cells to ensure each daughter cell receives a full set of chromosomes and complement of cytoplasm during mitosis. A human homolog of the Drosophila warts tumor suppressor, h-warts/LATS1, is an evolutionarily conserved serine/threonine kinase and a dynamic component of the mitotic apparatus We have identified an interaction of h-warts/LATS1 with zyxin, a regulator of actin filament assembly. Zyxin is a component of focal adhesion; however, during mitosis, a fraction of cytoplasmic-dispersed zyxin becomes associated with h-warts/LATS1 on the mitotic apparatus We found that zyxin is phosphorylated specifically during mitosis, most likely by Cdc2 kinase, and that the phosphorylation regulates association with h-warts/LATS1. Furthermore, microinjection of truncated h-warts/LATS1 protein, including the zyxin-binding portion, interfered with localization of zyxin to mitotic apparatus, and the duration of mitosis of these injected cells was significantly longer than that of control cells. These findings suggest that h-warts/LATS1 and zyxin play a crucial role in controlling mitosis progression by forming a regulatory complex on mitotic apparatus

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:358265 CAPLUS
DOCUMENT NUMBER: 133:100802
TITLE: mRNA expression patterns in different stages of asbestos-induced carcinogenesis in rats
AUTHOR(S): Sandhu, H.; Dehnen, W.; Roller, M.; Abel, J.; Unfried, K.
CORPORATE SOURCE: Department of Experimental Toxicology, Medical Institute of Environmental Hygiene at the Heinrich Heine University, Dusseldorf, 40225, Germany
SOURCE: Carcinogenesis (2000), 21(5), 1023-1029
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human malignant mesotheliomas are induced almost exclusively by fibrous dusts. The nature of interactions between fibers and target cells, and the mol. mechanisms leading to tumorigenesis, are not yet understood. Here, the mRNA expression patterns at different stages of asbestos-induced carcinogenesis in rats were monitored by suppression subtractive hybridization (SSH) and array assay. Several genes were upregulated in pre-tumorous tissues from asbestos-treated rats, in asbestos-induced tumors, and in cells treated with asbestos in vitro. The upregulation of the proto-oncogene c-myc, fra-1, and egfr in fiber-induced carcinogenesis was demonstrated at different stages of carcinogenesis. A possible role of Fra-1 as one of the dimeric proteins generating the AP-1 transcription factor was substantiated by its dose-dependent expression in mesothelial cells treated with asbestos in vitro. The upregulation of osteopontin (an extracellular matrix protein) and of zyxin and integrin-linked kinase (intracellular proteins associated with the focal adhesion contact) indicate that fibers may affect integrin-linked signal transduction and extracellular matrix proteins.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:85800 CAPLUS
DOCUMENT NUMBER: 132:234686
TITLE: LPP, an actin cytoskeleton protein related to zyxin, harbors a nuclear export signal and transcriptional activation capacity
AUTHOR(S): Petit, Marleen M. R.; Fradelizi, Julie; Golsteyn, Roy M.; Ayoubi, Torik A. Y.; Menichi, Bernadette; Louvard, Daniel; Van de Ven, Wim J. M.; Friederich, Evelyne
CORPORATE SOURCE: Laboratory for Molecular Oncology, Center for Human Genetics, University of Leuven and Flanders Interuniversity Institute for Biotechnology, Louvain, B-3000, Belg.
SOURCE: Molecular Biology of the Cell (2000), 11(1), 117-129
CODEN: MBCEEV; ISSN: 1059-1524
PUBLISHER: American Society for Cell Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The LPP gene is the preferred translocation partner of the HMGIC gene in a subclass of human benign mesenchymal tumors known as lipomas. Here we have characterized the LPP gene product that shares 41% of sequence identity with the focal adhesion protein zyxin. LPP localizes in focal adhesions as well as in cell-to-cell contacts, and it binds VASP, a protein implicated in the control of actin organization. In addition, LPP accumulates in the nucleus of cells upon treatment with leptomycin B, an inhibitor of the export factor CRM1. The nuclear export of LPP depends on an N-terminally located leucine-rich sequence that shares sequence homol. with well-defined nuclear export

signals. Moreover, LPP displays transcriptional activation capacity, as measured by GAL4-based assays. Altogether, these results show that the LPP protein has multifunctional domains and may serve as a scaffold upon which distinct protein complexes are assembled in the cytoplasm and in the nucleus.

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:331285 CAPLUS
DOCUMENT NUMBER: 129:77980
TITLE: The focal adhesion phosphoprotein, VASP
AUTHOR(S): Holt, Mark R.; Critchley, David R.; Brindle, Nicholas P. J.
CORPORATE SOURCE: Department of Biochemistry, University of Leicester, Leicester, LE1 7RH, UK
SOURCE: International Journal of Biochemistry & Cell Biology (1998), 30(3), 307-311
CODEN: IJBBFU; ISSN: 1357-2725
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 14 refs. Vasodilator-stimulated phosphoprotein (VASP) is associated with focal adhesions and areas of dynamic membrane activity, where it is thought to have an important role in actin filament assembly and cell motility. VASP contains a central proline-rich sequence which recruits the G-actin binding protein profilin. Localization of VASP to the leading edge of a migrating cell can lead to local accumulation of profilin, which in turn can supply actin monomers to growing filament ends. VASP binds to the focal adhesion proteins vinculin and zyxin and this probably directs the phosphoprotein to focal adhesions and the leading edge of stimulated cells. VASP functions as a binding intermediate between profilin and focal adhesion proteins. Intracellular pathogens, including Listeria monocytogenes, have coat proteins which bind VASP. This is one way in which these pathogens use VASP, and other proteins from the host cell, to assemble the actin filaments they require to move around the cytoplasm of infected cells and enter neighboring cells. Understanding the role of VASP and other proteins in cell and bacterial motility is likely to lead to development of new therapeutic strategies for diseases including atherosclerosis and tumor growth, and for limiting the spread of intracellular pathogens.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs 8-14

L6 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:168956 CAPLUS
DOCUMENT NUMBER: 128:281277
TITLE: Down-regulated proteins of mesenchymal tumor cells
AUTHOR(S): Schenker, Thomas; Trueb, Beat
CORPORATE SOURCE: MEM-Institute, Division of Biology, University of Bern, Bern, CH-3010, Switz.
SOURCE: Experimental Cell Research (1998), 239(1), 161-168
CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To identify proteins that are lost during the establishment of the transformed phenotype of a tumor cell, the authors have prepared a subtracted cDNA library with mRNA from normal human fibroblasts and from their matched SV40 transformed counterparts. More than 40 clones were obtained that showed a dramatic reduction in their relative expression after

oncogenic transformation. The proteins encoded by these clones could be grouped into four distinct classes: extracellular matrix proteins (fibronectin, βig-h3, collagen VI), enzymes (collagenase, urokinase), cytoskeletal proteins (vinculin, SM22) and regulatory proteins (β-glycan, integrin-associated protein, myosin kinase, IGFBP-5). Six novel gene products were discovered during these expts., including a novel serine protease, a zyxin-like protein, an ankyrin-like protein, and a GTP-binding protein. Only four of all the transformation-sensitive cDNAs were consistently down-regulated when a variety of cell lines derived from spontaneous mesenchymal tumors was investigated: βig-h3, collagen VI, the novel ankyrin-like protein, and IGFBP-5. It is likely that these gene products play an important role in the maintenance of the normal phenotype.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:124880 CAPLUS
DOCUMENT NUMBER: 118:124880
TITLE: Steroid derivatives with 2-propynyloxy group in position 3, useful as intermediates for radiotherapeutics, and method of their preparation
INVENTOR(S): Pouzar, Vladimir; Schneiderova, Lenka; Drasar, Pavel; Strouf, Oldrich; Havel, Miroslav
PATENT ASSIGNEE(S): Czech.
SOURCE: Czech., 6 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 267444	B1	19900212	CS 1988-5354	19880728

PRIORITY APPLN. INFO.: CS 1988-5354 19880728
OTHER SOURCE(S): MARPAT 118:124880
AB Steroids HC.tplbond.CCH2OR [I; R = 5-cholesten-3β-yl, 20-oxo-5-pregnen-3β-yl, 17-oxo-5-androsten-3β-yl, 17β-methoxymethoxy-5-androsten-3β-yl] were prepared as intermediates for steroidal [10B]-dicarbadodecaborane derivs., used for neutron-capture therapy of hormone-dependent tumors. I were prepared in 6-32% yield by reaction of corresponding alcs. ROH with 1-5 mol equiv HC.tplbond.CCH2Br in an organic solvent (especially 2:1 C6H6/MeCN), in the presence of a quaternary ammonium salt such as Bu4NHSO4 [mol ratio 1:(1-4) vs. ROH] and aqueous 10-19M NaOH at 10-70°.

L6 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:124878 CAPLUS
DOCUMENT NUMBER: 118:124878
TITLE: Steroid derivatives with 2-propynyloxy group in position 20, useful as intermediates for radiotherapeutics, and method of their preparation
INVENTOR(S): Pouzar, Vladimir; Schneiderova, Lenka; Drasar, Pavel; Strouf, Oldrich; Havel, Miroslav
PATENT ASSIGNEE(S): Czech.
SOURCE: Czech., 5 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

CS 267443	B1	19900212	CS 1988-5353	19880728
PRIORITY APPLN. INFO.:			CS 1988-5353	19880728

OTHER SOURCE(S): MARPAT 118:124878

AB Steroids HC.tplbond.CCH2OR [I; R = 3β-methoxymethoxy-21-nor-5-pregnen-20-yl, 3-oxo-21-nor-4-pregnen-20-yl] were prepared as intermediates for steroidal [10B]-dicarbadodecaborane derivs., used for neutron-capture therapy of hormone-dependent tumors. I were prepared in 10-32% yield by reaction of corresponding alcs. ROH with 1-5 mol equiv HC.tplbond.CCH2Br in an organic solvent (especially 2:1 C6H6/MeCN), in the presence of a quaternary ammonium salt such as Bu4NHSO4 [mol ratio 1:(1-4) vs. ROH] and aqueous 10-19M NaOH at 10-70°.

L6 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1993:124876 CAPLUS
DOCUMENT NUMBER: 118:124876
TITLE: Steroid derivatives with 2-propynyloxy group in position 17, useful as intermediates for radiotherapeutics, and method of their preparation
INVENTOR(S): Pouzar, Vladimir; Schneiderova, Lenka; Drasar, Pavel; Strouf, Oldrich; Havel, Miroslav
PATENT ASSIGNEE(S): Czech.
SOURCE: Czech., 6 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 267442	B1	19900212	CS 1988-5351	19880728
PRIORITY APPLN. INFO.:			CS 1988-5351	19880728

OTHER SOURCE(S): MARPAT 118:124876

AB Steroids HC.tplbond.CCH2OR [I; R = 3-(2-tetrahydropyranyloxy)-1,3,5(10)-estratrien-17β-yl, 3β-methoxymethoxy-5-androsten-17β- or -17α-yl, 3β-(2-tetrahydropyranyloxy)-5-androsten-17β-yl, 3-oxo-4-androsten-17β-yl] were prepared as intermediates for steroidal [10B]-dicarbadodecaborane derivs., used for neutron-capture therapy of hormone-dependent tumors. I were prepared in 8-32% yield by reaction of corresponding alcs. ROH with 1-5 mol equiv HC.tplbond.CCH2Br in an organic solvent (especially 2:1 C6H6/MeCN), in the presence of a quaternary ammonium salt such as Bu4NHSO4 [mol ratio 1:(1-4) vs. ROH] and aqueous 10-19M NaOH at 10-70°.

L6 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

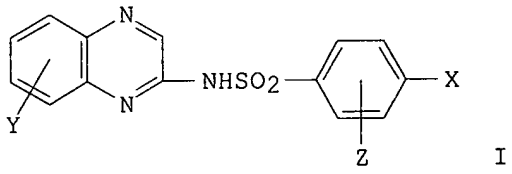
ACCESSION NUMBER: 1991:159979 CAPLUS
DOCUMENT NUMBER: 114:159979
TITLE: Potential new photosensitizers for photodynamic therapy
AUTHOR(S): Ho, Yau Kwan; Pandey, Ravindra K.; Sumlin, Adam B.; Missert, Joseph R.; Bellnier, David A.; Dougherty, Thomas J.
CORPORATE SOURCE: Oncol. Found. Buffalo, Buffalo, NY, 14203, USA
SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (1990), 1203(Proc. Photodyn. Ther.: Mech. 2, 1990), 293-300
CODEN: PSISDG; ISSN: 0277-786X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The production and tumor photosensitizing effects of 3 new photosensitizers, i.e., bis(dimethylhydroxypropylsiloxy)silicon naphthalocyanine, bis(dimethylacetoxypropylsiloxy)silicon naphthalocyanine, and especially 2-(1-O-hexyl)ethyldesvinylmethylpheophorbide a, were examined

L6 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:169038 CAPLUS
DOCUMENT NUMBER: 106:169038
TITLE: Quinoxaline derivatives as neoplasm inhibitors
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62000426	A	19870106	JP 1986-146277	19860624
EP 215200	A2	19870325	EP 1986-108295	19860618
EP 215200	A3	19890802		
EP 215200	B1	19920909		
R: CH, DE, FR, GB, IT, LI, NL				
CA 1267604	A1	19900410	CA 1986-511938	19860619
US 4931433	A	19900605	US 1987-45256	19870501
PRIORITY APPLN. INFO.:			US 1985-748070 A	19850624
			US 1986-858092 B1	19860429

OTHER SOURCE(S): MARPAT 106:169038
GI



I

AB Quinoxaline derivs. I (Y = NO2, OMe, H, Cl, Br, OH; X = NO2, NH2, acylamido, NH(CH2)nCOOH, NHCH2SO3H; Z = H or halo), especially 2-sulfonylamino-5-chloroquinoxaline (II), are neoplasm inhibitors as determined by the Sheamaker method (1985). In vivo, II (200-449 mg/kg/day) prolonged the life span of mice transplanted with human LOX melanin-deficient melanocarcinoma.

L6 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:405881 CAPLUS
DOCUMENT NUMBER: 99:5881
TITLE: Isoprenylamine derivatives and their acid addition salts
INVENTOR(S): Tahara, Yoshiyuki; Komatsu, Yasuhiro; Koyama, Hiroyasu; Kubota, Reiko; Yamaguchi, Teruhito; Takahashi, Toshihiro
PATENT ASSIGNEE(S): Nisshin Flour Milling Co., Ltd., Japan
SOURCE: Ger. Offen., 27 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3218822	A1	19821202	DE 1982-3218822	19820518
DE 3218822	C2	19901018		
JP 57192340	A	19821126	JP 1981-76155	19810518

```
     JP 01028736           B     19890605
     US 4568765            A     19860204    US 1982-377577          19820512
     GB 2098613            A     19821124    GB 1982-14242           19820517
     GB 2098613            B     19850109
     FR 2505824            A1    19821119    FR 1982-8704            19820518
     FR 2505824            B1    19860425
PRIORITY APPLN. INFO.:                        JP 1981-76155       A   19810518
OTHER SOURCE(S):          CASREACT 99:5881; MARPAT 99:5881
AB   H(CH2CRMeCHR1CH2)n[NR2(CH2)p]qNHR2 (n = 2-10; p = 2 or 3; q ≥2,
     especially 2 or 3; R, R1 = H, H or bond; R2 = H, Bz, PhCH2 or
     lower alkyl or acyl) were prepared Thus decaprenyl bromide reacted with
     triethylenetetramine to give, via the tetrakis(trifluoroacetyl) derivative,
     H(CH2CMe:CHCH2)10(NHCH2CH2)3NH2, which provided 87.9% protection against
     Vaccinia infections and gave increased survival times in 5/6 of cases
     against KN7-8 tumor cells in mice.


=> file dissab
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      72.12      72.33

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)            SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                     -10.92     -10.92

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=> s ESP-2 or HED-2 or Zyxin or Zyxin-2
           381 ESP
            19 ESPS
           388 ESP
                 (ESP OR ESPS)
        380284 2
             2 ESP-2
                 (ESP(W)2)
            32 HED
             2 HEDS
            33 HED
                 (HED OR HEDS)
        380284 2
             0 HED-2
                 (HED(W)2)
            10 ZYXIN
            10 ZYXIN
        380284 2
             0 ZYXIN-2
                 (ZYXIN(W)2)
L7          12 ESP-2 OR HED-2 OR ZYXIN OR ZYXIN-2

=> s cancer? or tumor? or neoplas?
         17132 CANCER?
         14172 TUMOR?
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          2482 NEOPLAS?
L8       27419 CANCER? OR TUMOR? OR NEOPLAS?

=> s l7 and l8
L9           2 L7 AND L8

=> d ibib 1-2

L9   ANSWER 1 OF 2  DISSABS COPYRIGHT (C) 2007 ProQuest Information and
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ACCESSION NUMBER:   2001:26596  DISSABS   Order Number: AAI9988630
TITLE:              Characterization of TRIP6, a new zyxin family
                    member
AUTHOR:             Yi, Jinseong [Ph.D.]; Beckerle, Mary C. [adviser]
CORPORATE SOURCE:   The University of Utah (0240)
SOURCE:             Dissertation Abstracts International, (2000) Vol. 61, No.
                    9B, p. 4521. Order No.: AAI9988630. 160 pages.
                    ISBN: 0-599-95237-7.
DOCUMENT TYPE:      Dissertation
FILE SEGMENT:       DAI
LANGUAGE:           English

L9   ANSWER 2 OF 2  DISSABS COPYRIGHT (C) 2007 ProQuest Information and
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ACCESSION NUMBER:   2000:35209  DISSABS   Order Number: AAI9956453
TITLE:              Regulation of the cytoskeleton in human microvascular
                    endothelial cells
AUTHOR:             Zimmerman, Matthew John [Ph.D.]; Feramisco, James R.
                    [adviser]
CORPORATE SOURCE:   University of California, San Diego (0033)
SOURCE:             Dissertation Abstracts International, (2000) Vol. 61, No.
                    1B, p. 52. Order No.: AAI9956453. 139 pages.
DOCUMENT TYPE:      Dissertation
FILE SEGMENT:       DAI
LANGUAGE:           English


=> s therap? or treat? or inhibit? or suppres?
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        163294 TREAT?
         67152 INHIBIT?
         23440 SUPPRES?
L10     248978 THERAP? OR TREAT? OR INHIBIT? OR SUPPRES?

=> s l9 and l10
L11          1 L9 AND L10

=> d ibib abs kwic

L11  ANSWER 1 OF 1  DISSABS COPYRIGHT (C) 2007 ProQuest Information and
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ACCESSION NUMBER:   2000:35209  DISSABS   Order Number: AAI9956453
TITLE:              Regulation of the cytoskeleton in human microvascular
                    endothelial cells
AUTHOR:             Zimmerman, Matthew John [Ph.D.]; Feramisco, James R.
                    [adviser]
CORPORATE SOURCE:   University of California, San Diego (0033)
SOURCE:             Dissertation Abstracts International, (2000) Vol. 61, No.
                    1B, p. 52. Order No.: AAI9956453. 139 pages.
DOCUMENT TYPE:      Dissertation
FILE SEGMENT:       DAI
LANGUAGE:           English
AB        Angiogenesis is required for the growth of solid tumors.
     VEGF, by virtue of an expression pattern of receptors restricted mainly to
     the endothelium, is a critical regulator of angiogenesis in vivo.
```

Representational difference analysis was utilized to clone genes that were upregulated in endothelial cells 2 hours after treatment with VEGF. Two genes, fra-1 and TR3, both themselves regulators of transcription, were found to be upregulated 3.1 and 1.4 fold respectively. A third gene product, zyxin, was found to localize with focal adhesions and stress fibers after

VEGF treatment, in contrast to the effects of another angiogenic factor, 12-tetradeconoylphorbol 13-acetate (TPA), which caused loss of zyxin localization to these structures. Loss of zyxin at stress fibers and focal adhesions over time and dose of TPA treatment correlated with a reduced electrophoretic mobility of zyxin on polyacrylamide gels which was determined to be due to phosphorylation of the protein. Both effects were blocked by inhibition of PKC activity. Inhibition of MEK activity, however, inhibited zyxin phosphorylation downstream of TPA treatment, but not loss of zyxin at focal adhesions and stress fibers, indicating that zyxin phosphorylation could be decoupled from the cytoskeletal rearrangements induced by TPA. Introduction of inactivated cdc42 into HMvECs paralleled the effect of VEGF increased localization of zyxin to actin stress fibers and focal adhesions, an effect which may be mediated by the inactivation of the downstream effector PAK. Inactivation of PAK alone and in combination with activated cdc42 increased stress fiber formation in HMvECs, supporting the hypothesis that PAK mediates stress fiber breakdown. However, PAK inactivation is also predicted to inhibit LIM-kinase, and inhibition of LIM-kinase by independent means inhibited, not cooperated with, the phenotype induced by activated cdc42. These apparently contradictory results my be explained by alternate emerging regulatory pathways.

AB Angiogenesis is required for the growth of solid tumors. VEGF, by virtue of an expression pattern of receptors restricted mainly to the endothelium, is a critical regulator of angiogenesis in vivo. Representational difference analysis was utilized to clone genes that were upregulated in endothelial cells 2 hours after treatment with VEGF. Two genes, fra-1 and TR3, both themselves regulators of transcription, were found to be upregulated 3.1 and 1.4 fold respectively. A third gene product, zyxin, was found to localize with focal adhesions and stress fibers after

VEGF treatment, in contrast to the effects of another angiogenic factor, 12-tetradeconoylphorbol 13-acetate (TPA), which caused loss of zyxin localization to these structures. Loss of zyxin at stress fibers and focal adhesions over time and dose of TPA treatment correlated with a reduced electrophoretic mobility of zyxin on polyacrylamide gels which was determined to be due to phosphorylation of the protein. Both effects were blocked by inhibition of PKC activity. Inhibition of MEK activity, however, inhibited zyxin phosphorylation downstream of TPA treatment, but not loss of zyxin at focal adhesions and stress fibers, indicating that zyxin phosphorylation could be decoupled from the cytoskeletal rearrangements induced by TPA. Introduction of inactivated cdc42 into HMvECs paralleled the effect of VEGF increased localization of zyxin to actin stress fibers and focal adhesions, an effect which may be mediated by the inactivation of the downstream effector. . . fiber formation in HMvECs, supporting the hypothesis that PAK mediates stress fiber breakdown. However, PAK inactivation is also predicted to inhibit LIM-kinase, and inhibition of LIM-kinase by independent means inhibited, not cooperated with, the phenotype induced by activated cdc42. These apparently contradictory results my be explained by alternate emerging regulatory. . .

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CONFIRMATION NO. 2270

SERIAL NUMBER	FILING OR 371(c) DATE / RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
10/740,266	12/18/2003	435	1642	1417-03

APPLICANTS

Christian Auclair, Paris, FRANCE;
Valerie Amsellem, Paris, FRANCE;
Martial Hervy, Paris, FRANCE;
Frederic Subra, Paris, FRANCE;

**** CONTINUING DATA ***************************

This application is a CON of PCT/FR02/02106 06/18/2002

**** FOREIGN APPLICATIONS *********************

FRANCE 01/07976 06/18/2001

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** 04/22/2004

Foreign Priority claimed	35 USC 119 (a-d) conditions met	Verified and Acknowledged	STATE OR COUNTRY	SHEETS DRAWING	TOTAL CLAIMS	INDEPENDENT CLAIMS
☑ yes ☐ no	☑ yes ☐ no ☐ Met after Allowance	Examiner's Signature / Initials	FRANCE	17	47	9

ADDRESS
35811

TITLE
Pharmaceutical composition for the diagnosis, prevention or treatment of a tumoral pathology comprising an agent modulating the polymerization state of actin

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☐	L38	l35.ab. or l35.clm.	16
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☐	L35	ESP-2 or HED-2 or Zyxin or Zyxin-2	220
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☐	L33	L3 and L21	79
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☐	L25	s L17.ab.	1
☐	L24	L21 and L16	919
☐	L23	L21 and L19	23
☐	L22	L21 and L20	25
☐	L21	ewing$ NEAR2 sarcoma	2520
☐	L20	zyxin	203
☐	L19	cofilin	261
☐	L18	L17 and L14	5
☐	L17	actin	30701
☐	L16	actin	30701
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☐	L14	(auclair or amsellem or hervy or subra).in.	397
☐	L13	L12 or L11 or L10	25539
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☐	L4	L3 and ewing$	111
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☐	L2	L1 and ewing$	1
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NEWS	5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
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NEWS	11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS	12	FEB 27	New STN AnaVist pricing effective March 1, 2006
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NEWS	15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	16	MAR 01	INSPEC reloaded and enhanced
NEWS	17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS	18	MAR 08	X.25 communication option no longer available after June 2006
NEWS	19	MAR 22	EMBASE is now updated on a daily basis
NEWS	20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS	21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS	22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS	23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS	24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS	25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

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DICTIONARY FILE UPDATES: 16 APR 2006 HIGHEST RN 880543-27-1

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E1 1 DOLASETRON MESYLATE/CN
E2 1 DOLASTANE/CN
E3 0 --> DOLASTATIN/CN
E4 1 DOLASTATIN 1/CN
E5 1 DOLASTATIN 10/CN
E6 1 DOLASTATIN 11/CN
E7 1 DOLASTATIN 12/CN
E8 1 DOLASTATIN 13/CN
E9 1 DOLASTATIN 13,
4-(3-AMINO-3,4-DIHYDRO-2-OXO-A-(PHENYLMETHYL)-1(2H)-PYRIDINEACETIC ACID)-/CN
E10 1 DOLASTATIN 13,
4-(3-AMINO-3,4-DIHYDRO-6-HYDROXY-2-OXO-A-(PHENYLMETHYL)-1(2H)-PYRIDINEACETIC ACID)-/CN
E11 1 DOLASTATIN 14/CN
E12 1 DOLASTATIN 15/CN

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E14          1      DOLASTATIN 17/CN
E15          1      DOLASTATIN 17 (DOLABELLA AURICULARIA)/CN
E16          1      DOLASTATIN 18/CN
E17          1      DOLASTATIN 19/CN
E18          1      DOLASTATIN 2/CN
E19          1      DOLASTATIN 3/CN
E20          1      DOLASTATIN 4/CN
E21          1      DOLASTATIN 5/CN
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E25          1      DOLASTATIN 9/CN

=> S E6
L1           1 "DOLASTATIN 11"/CN

=> DIS L1 1 SQIDE
THE ESTIMATED COST FOR THIS REQUEST IS 6.36 U.S. DOLLARS
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L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   111517-68-1  REGISTRY
CN   Cyclo[L-alanyl-(2S,3R)-3-amino-2-methylpentanoyl-(2S,3S)-2-hydroxy-3-
     methylpentanoylglycyl-N-methyl-L-leucylglycyl-N-methyl-L-valyl-N,O-
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CN   1-Oxa-4,7,10,13,16,19,24,27-octaazacyclotriacontane, cyclic peptide deriv.
CN   Dolastatin 11
OTHER NAMES:
CN   NSC 606195
FS   PROTEIN SEQUENCE; STEREOSEARCH
SQL  8
NTE  modified (modifications unspecified)
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uncommon	Oaa-6	-	-
uncommon	Oaa-8	-	-

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SR   CA
LC   STN Files:   BEILSTEIN*, BIOSIS, CA, CAPLUS, NAPRALERT, TOXCENTER,
       USPATFULL
         (*File contains numerically searchable property data)
DT.CA  CAplus document type:  Dissertation; Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); PROC (Process); PRP
       (Properties); USES (Uses)
RL.NP  Roles from non-patents:  BIOL (Biological study); PREP (Preparation);
       PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents:  PREP
       (Preparation); PRP (Properties)
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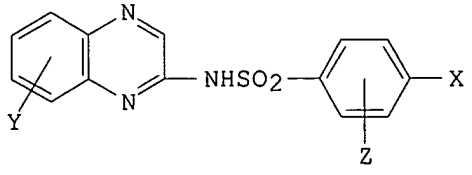

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22 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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FULL ESTIMATED COST	12.00	12.21

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49670 ACTIN
30327 ACTINS
L2 52669 ACTIN
(ACTIN OR ACTINS)

=> s cofilin
775 COFILIN
232 COFILINS
L3 812 COFILIN
(COFILIN OR COFILINS)

=> s antag? or inhibit?
281605 ANTAG?
1822219 INHIBIT?
L4 1968300 ANTAG? OR INHIBIT?

=> s l4 (l) l3
L5 222 L4 (L) L3

=> s ewing?
L6 1659 EWING?

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=> s l6 and l5
L7            1 L6 AND L5

=> d ibib

L7   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2002:977858  CAPLUS
DOCUMENT NUMBER:          138:52333
TITLE:                    Pharmaceutical composition for diagnosis, prevention
                          or treatment of a tumorous state, comprising a
                          modulator of the actin polymerization state
INVENTOR(S):              Auclair, Christian; Amsellem, Valerie; Hervy, Martial;
                          Subra, Frederic
PATENT ASSIGNEE(S):       Bioalliance Pharma, Fr.; Ecole Normale Superieure De
                          Cachan; Institut Gustave Roussy-IGR; Centre National
                          de la Recherche Scientifique CNRS
SOURCE:                   PCT Int. Appl., 68 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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     WO 2002102846         A2    20021227    WO 2002-FR2106           20020618
     WO 2002102846         A3    20040422
     WO 2002102846         B1    20040603
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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             GN, GQ, GW, ML, MR, NE, SN, TD, TG
     FR 2825928            A1    20021220    FR 2001-7976             20010618
     FR 2825928            B1    20040402
     CA 2450845            AA    20021227    CA 2002-2450845          20020618
     EP 1432732            A2    20040630    EP 2002-745538           20020618
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     JP 2005504521         T2    20050217    JP 2003-506318           20020618
     US 2004191230         A1    20040930    US 2003-740266           20031218
PRIORITY APPLN. INFO.:                       FR 2001-7976         A   20010618
                                             WO 2002-FR2106       W   20020618


=> s l1
L8           22 L1

=> s l8 and l6
L9            0 L8 AND L6

=> s zyxin
            219 ZYXIN
             28 ZYXINS
L10         224 ZYXIN
                (ZYXIN OR ZYXINS)

=> s l10 and l6
L11           3 L10 AND L6
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L11 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:184733 CAPLUS
DOCUMENT NUMBER: 142:371546
TITLE: The actin cytoskeleton-associated protein zyxin acts as a tumor suppressor in Ewing tumor cells
AUTHOR(S): Amsellem, Valerie; Kryszke, Marie-Helene; Hervy, Martial; Subra, Frederic; Athman, Rafika; Leh, Herve; Brachet-Ducos, Corinne; Auclair, Christian
CORPORATE SOURCE: CNRS UMR 8113, Laboratoire de Biotechnologie et Pharmacologie genetique appliquee, Ecole Normale Superieure de Cachan, Cachan, 94230, Fr.
SOURCE: Experimental Cell Research (2005), 304(2), 443-456
CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:583223 CAPLUS
DOCUMENT NUMBER: 141:188806
TITLE: Molecular mechanisms of CD99-induced caspase-independent cell death and cell-cell adhesion in Ewing's sarcoma cells: actin and zyxin as key intracellular mediators
AUTHOR(S): Cerisano, Vanessa; Aalto, Yan; Perdichizzi, Stefania; Bernard, Ghislaine; Manara, Maria Cristina; Benini, Stefania; Cenacchi, Giovanna; Preda, Paola; Lattanzi, Giovanna; Nagy, Balint; Knuutila, Sakari; Colombo, Mario Paolo; Bernard, Alain; Picci, Piero; Scotlandi, Katia
CORPORATE SOURCE: Laboratorio di Ricerca Oncologica, Istituti Ortopedici Rizzoli, Bologna, 40136, Italy
SOURCE: Oncogene (2004), 23(33), 5664-5674
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:977858 CAPLUS
DOCUMENT NUMBER: 138:52333
TITLE: Pharmaceutical composition for diagnosis, prevention or treatment of a tumorous state, comprising a modulator of the actin polymerization state
INVENTOR(S): Auclair, Christian; Amsellem, Valerie; Hervy, Martial; Subra, Frederic
PATENT ASSIGNEE(S): Bioalliance Pharma, Fr.; Ecole Normale Superieure De Cachan; Institut Gustave Roussy-IGR; Centre National de la Recherche Scientifique CNRS
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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     WO 2002102846         A2    20021227    WO 2002-FR2106         20020618
     WO 2002102846         A3    20040422
     WO 2002102846         B1    20040603
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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             GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
             GN, GQ, GW, ML, MR, NE, SN, TD, TG
     FR 2825928            A1    20021220    FR 2001-7976           20010618
     FR 2825928            B1    20040402
     CA 2450845            AA    20021227    CA 2002-2450845        20020618
     EP 1432732            A2    20040630    EP 2002-745538         20020618
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2005504521         T2    20050217    JP 2003-506318         20020618
     US 2004191230         A1    20040930    US 2003-740266         20031218
PRIORITY APPLN. INFO.:                       FR 2001-7976        A  20010618
                                             WO 2002-FR2106      W  20020618


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L5           222 S L4 (L) L3
L6          1659 S EWING?
L7             1 S L6 AND L5
L8            22 S L1
L9             0 S L8 AND L6
L10          224 S ZYXIN
L11            3 S L10 AND L6

=> s l3 and l6
L12            6 L3 AND L6

=> s l12 and l4
L13            4 L12 AND L4

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L13  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:248644  CAPLUS
DOCUMENT NUMBER:          142:274057
TITLE:                    Sequences of human schizophrenia related genes and use
                          for diagnosis, prognosis and therapy
INVENTOR(S):              Liew, Choong-chin
PATENT ASSIGNEE(S):       Chondrogene Limited, Can.
SOURCE:                   U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S.
                          Ser. No. 802,875.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
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LANGUAGE: English
FAMILY ACC. NUM. COUNT: 47
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004241727	A1	20041202	US 2004-812731		20040330
US 2004014059	A1	20040122	US 2002-268730		20021009
US 2005191637	A1	20050901	US 2004-803737		20040318
US 2005196762	A1	20050908	US 2004-803759		20040318
US 2005196763	A1	20050908	US 2004-803857		20040318
US 2005196764	A1	20050908	US 2004-803858		20040318
US 2005208505	A1	20050922	US 2004-803648		20040318
US 2004241727	A1	20041202	US 2004-812731		20040330
PRIORITY APPLN. INFO.:			US 1999-115125P	P	19990106
			US 2000-477148	B1	20000104
			US 2002-268730	A2	20021009
			US 2003-601518	A2	20030620
			US 2004-802875	A2	20040312
			US 2004-812731	A	20040330

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:248643 CAPLUS
DOCUMENT NUMBER: 142:274056
TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 47
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004241727	A1	20041202	US 2004-812731		20040330
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PRIORITY APPLN. INFO.:			US 1999-115125P	P	19990106
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			US 2003-601518	A2	20030620
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			US 2004-812731	A	20040330

L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:60754 CAPLUS
Correction of: 2004:1036571
DOCUMENT NUMBER: 142:233342
Correction of: 142:16836
TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 29
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004241727	A1	20041202	US 2004-812731	20040330
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US 2005191637	A1	20050901	US 2004-803737	20040318
US 2005196762	A1	20050908	US 2004-803759	20040318
US 2005196763	A1	20050908	US 2004-803857	20040318
US 2005196764	A1	20050908	US 2004-803858	20040318
US 2005208505	A1	20050922	US 2004-803648	20040318
US 2004265869	A1	20041230	US 2004-812716	20040330
US 2005208519	A1	20050922	US 2004-989191	20041115
PRIORITY APPLN. INFO.:			US 1999-115125P	P 19990106
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			US 2003-601518	A2 20030620
			US 2004-802875	A2 20040312
			US 2004-812731	A2 20040330
			WO 2004-US20836	A2 20040621

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:977858 CAPLUS
DOCUMENT NUMBER: 138:52333
TITLE: Pharmaceutical composition for diagnosis, prevention or treatment of a tumorous state, comprising a modulator of the actin polymerization state
INVENTOR(S): Auclair, Christian; Amsellem, Valerie; Hervy, Martial; Subra, Frederic
PATENT ASSIGNEE(S): Bioalliance Pharma, Fr.; Ecole Normale Superieure De Cachan; Institut Gustave Roussy-IGR; Centre National de la Recherche Scientifique CNRS
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002102846	B1	20040603		
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EP 1432732	A2	20040630	EP 2002-745538	20020618
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US 2004191230	A1	20040930	US 2003-740266	20031218

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L7             1 S L6 AND L5
L8            22 S L1
L9             0 S L8 AND L6
L10          224 S ZYXIN
L11            3 S L10 AND L6
L12            6 S L3 AND L6
L13            4 S L12 AND L4

=> s phosphoinositol?
L14          989 PHOSPHOINOSITOL?

=> s l14 and l6
L15            0 L14 AND L6

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               2 PHOSPHOTIDYLINOSITOLS
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                 (PHOSPHOTIDYLINOSITOL OR PHOSPHOTIDYLINOSITOLS)

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                                                   ENTRY    SESSION
FULL ESTIMATED COST                                29.78      41.99

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FILE LAST UPDATED:          11 APR 2006      <20060411/UP>
MOST RECENT UPDATE WEEK:        200614        <200614/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
    SEE
    http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE
    (last updated April 10, 2006) <<<

=> s cofilin
             179 COFILIN
              12 COFILINS
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L18         188 COFILIN
                (COFILIN OR COFILINS)

=> s ewing?
L19        3185 EWING?

=>

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L20          19 L19 AND L18

=> s antag? or inhibit?
          53720 ANTAG?
         189862 INHIBIT?
L21      198141 ANTAG? OR INHIBIT?

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L23           4 L22 NOT PY>2001

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L23    ANSWER 1 OF 4     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2001055168 PCTFULL  ED 20020827
TITLE (ENGLISH):         NUCLEIC ACIDS, PROTEINS AND ANTIBODIES
TITLE (FRENCH):          ACIDES NUCLEIQUES, PROTEINES, ET ANTICORPS
INVENTOR(S):             ROSEN, Craig, A.;
                         BARASH, Steven, C.;
                         RUBEN, Steven, M.
PATENT ASSIGNEE(S):      HUMAN GENOME SCIENCES, INC.;
                         ROSEN, Craig, A.;
                         BARASH, Steven, C.;
                         RUBEN, Steven, M.
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
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                         WO 2001055168         A1 20010802
DESIGNATED STATES
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                         CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:       WO 2001-US1331        A  20010117
PRIORITY INFO.:          US 2000-60/179,065       20000131
                         US 2000-60/180,628       20000204
                         US 2000-60/184,664       20000224
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                         US 2000-60/189,874       20000316
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                         US 2000-60/198,123       20000418
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US 2000-60/249,209	20001117
US 2000-60/250,160	20001201
US 2000-60/250,391	20001201
US 2000-60/256,719	20001205
US 2000-60/251,030	20001205
US 2000-60/251,988	20001205
US 2000-60/251,479	20001206
US 2000-60/251,869	20001208
US 2000-60/251,856	20001208
US 2000-60/251,868	20001208
US 2000-60/251,990	20001208
US 2000-60/251,989	20001208
US 2000-60/254,097	20001211
US 2001-60/259,678	20010105

L23 ANSWER 2 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999051766 PCTFULL ED 20020515
TITLE (ENGLISH): METHODS FOR PRODUCING LIBRARIES OF EXPRESSIBLE GENE SEQUENCES
TITLE (FRENCH): METHODES DE PRODUCTION DE BANQUES DE SEQUENCES DE GENES EXPRIMABLES
INVENTOR(S): FERNANDEZ, Joseph, Manuel;

HEYMAN, John, Alastair;
HOEFFLER, James, Paul;
MARKS-HULL, Heather, Lynn;
SINDICI, Michelle, Lynn

PATENT ASSIGNEE(S): INVITROGEN;
FERNANDEZ, Joseph, Manuel;
HEYMAN, John, Alastair;
HOEFFLER, James, Paul;
MARKS-HULL, Heather, Lynn;
SINDICI, Michelle, Lynn

LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9951766	A1	19991014

DESIGNATED STATES
W: AU CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.: WO 1999-US7270 A 19990402
PRIORITY INFO.: US 1998-09/054,936 19980403

L23 ANSWER 3 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999051620 PCTFULL ED 20020515
TITLE (ENGLISH): LIBRARIES OF EXPRESSIBLE GENE SEQUENCES
TITLE (FRENCH): BANQUES DE SEQUENCES DE GENES POUVANT ETRE EXPRIMEES
INVENTOR(S): FERNANDEZ, Joseph, Manuel;
HEYMAN, John, Alastair;
HOEFFLER, James, Paul

PATENT ASSIGNEE(S): INVITROGEN
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9951620	A1	19991014

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.: WO 1999-US7334 A 19990402
PRIORITY INFO.: US 1998-60/080,626 19980403
US 1998-60/096,981 19980818

L23 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1998041648 PCTFULL ED 20020514
TITLE (ENGLISH): TARGET GENES FOR ALLELE-SPECIFIC DRUGS
TITLE (FRENCH): GENES CIBLES POUR MEDICAMENTS SPECIFIQUES D'ALLELES
INVENTOR(S): HOUSMAN, David;
LEDLEY, Fred, D.;
STANTON, Vincent, P., Jr.

PATENT ASSIGNEE(S): VARIAGENICS, INC.;
HOUSMAN, David;
LEDLEY, Fred, D.;
STANTON, Vincent, P., Jr.

LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9841648	A2	19980924

DESIGNATED STATES
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW AT BE CH DE

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                        DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.:      WO 1998-US5419       A  19980319
PRIORITY INFO.:         US 1997-60/041,057      19970320


=> d kwic 2

L23    ANSWER 2 OF 4     PCTFULL   COPYRIGHT 2006 Univentio on STN

DETD  .  .  .  U3 52.36 60
      snoRNP associated 55 kDa
      protein
      GI H-DO0096 Transtyretin (prealbumin) 16.28 20
      C4 H-DO0408 Cytochrome P450 IIIA7 (P450- 55.44 64
      HFLa)
      M302 E7 H-DO0682 cofilin 18.37 30
      M383 G2 H-DO0726 ferrochelatase 46.64 50.OkDa
      M383 C3 H-DO0760 proteasome, subunit HO 25.85 34.OkDa
      M305 B4 H-DO0761 proteasome, subunit HC5 26.62.  .  .
 .  .  .
      enoyl-Coenzyme A hydratase, 32.01 58
      short chain, mitochondrial
      El H-DI4446 Human HFREP- I mRNA for 34.43 40
      unknown protein, complete cds
      167-14 H-DI4497 H.sapiens (Ewing's sarcoma cell 51.44 64
      line) mRNA encoding open
      reading frame
      M266 D2 H-DI4520 basic transcription element- 24.2 33.OkDa
      binding protein 2
      M318 D2 H-DI4658 hypothetical.  .  .
 .  .  .
      42.79 48
      M298 C2 H-JO2611 apolipoprotein D 20.9 3 I.OkDa
      M266 C4 H-JO2683 ADP/ATP carrier protein 32.89 36
      M383 H2 H-JO2685 plasminogen activator inhibitor, 45.76
      50.OkDa
      placenta
      167-3 H-JO2853 casein kinase 11, alpha chain 43.08 50
      E3 H-JO2854 Human 20-kDa myosin light 19.03 31
      chain (MLC-2) mRNA, complete
      cds
      M248.  .  .
 .  .  .
      transaldolase 37.18 39.OkDa
      M423 C4 H-LI9593 Interleukin 8 receptor, beta 39.71 4 1.0kDa
      G I H-LI9686 Homo sapiens macrophage 12.76 1 3
      migration inhibitory factor (MIF)
      gene, complete cds
      G2 H-LI9739 metallopanstimulin 1 9.35 32
      M302 E3 H-LI9871 activating transcription factor 3 20.02 36.OkDa
      167-86 H-L20422 14 3 protein eta 34 1 3
      M440 B2 H-L20492 Human garmna-glutamyl 24.86 35.OkDa
      transpeptidase mRNA, complete
      cds
      M315 BI H-L20688 GDP-dissociation inhibitor 22.22 32
      protein rhoA
      M271 H3 H-L20941 ferritin, heavy polypeptide. 20.24 32
      FERRITIN IS AN
      INTRACELLULAR,
      MOLECULE THAT STORES
      IRON IN A SOLUBLE,
      NONTOXIC, READILY
      AVAILABLE FORM.
 .  .  .
      30
```

transforming protein rhoC,
Aplysia ras-related hornolog 9
M236 E3 H-L25085 Sec6l complex, beta subunit, 10.67 19
PROTEIN TRANSLOCATION
TN THE ENDOPLASMIC
RETICULUM
167-85 H-1,25610 cyclin-dependent kinase inhibitor 32
B2 H-L25610 cyclin-dependent kinase inhibitor 18.110 40
1
M297 H2 H-1,26232 cathepsin A/phospholipid transfer 54.34 64.OkDa
protein
167-4 H-1,26318 stress-activated protein kinase 52 42.31
JNKI
M428 Fl H-1,27586 Human TR4 orphan. . .
. . .
E2 H-MI9713 tropomyosin, alpha, muscle 31.35 4I.OkDa
167-79 H-MI9722 proto-oncogene tyrosine-protein 64 58.26
kinase FGR
M248 HI H-M20560 Annexin III (lipocortin III), 35.64 37
INHIBITOR OF
PHOSPHOLIPASE A2
M235 HI H-M20681 GLUCOSE TRANSPORTER 54.67 50
TYPE 3, BRAIN
167-29 H-M21616 beta platelet-derived growth 121 121.7
factor receptor precursor
M305 A3 H-M21812. . .
. . .
palmitoylated membrane protein, 51.37 5 I.OkDa
erythrocyte, 55 kDa
M302 C7 H-M65292 complement factor H-related 36.41 50
protein (GB:M65292)
D3 H-M68516 Human protein C inhibitor gene, 44.77 54
complete cds
167-27 H-M68520 cell division protein kinase 2 38 32.85
M236 D5 H-M68867 Cellular retinoic acid-binding 15.29 19.OkDa
protein 2,. . .
. . .
Al H-PO 197 S-adenosyhnethionine synthetase 42.46
2 (metX)
M365 BI H-PO203 hypothetical protein 10.12
M365 Cl H-PO209 hypothetical protein 49.61
M365 DI H-PO213 glucose inhibited division protein 68.42
(gidA)
M381 El H-PO218 hypothetical protein 20.24
M365 El H-PO221 nifLJ-Iike protein 35.97
M365 F1 H-PO227 outer m mbrane protein (omp5). . . C2 P]3 -]]
ribosomal protein SI (rps 1)
M366 D2 H-PO403 phenylalanyl-tRNA synthetase, 36.19
alpha subunit (pheS)
M366 E2 H-PO404 protein kinase C inhibitor 11.55
(SP:PI6436)
M366 F2 H-PO405 nifS-like protein 48.51
M366 G2 H-PO406 hypothetical protein 21.67
M366 H2 H-PO407 biotin sulfoxide reductase (bisC) 87.67
M381 DI H-PO409. . .
. . .
alanine racemase, biosynthetic 41.58
(a
M371 D6 H-PO942 D-alanine glycine perinease 49.61
(dagA)
M371 E6 H-PO943 D-arnino acid dehydrogenase 45.21
(dadA)
M371 F6 H-PO944 translation initiation inhibitor, 13.86
putative
M371 G6 H-PO946 conserved hypothetical integral 54.67

membrane protein
M371 H6 H-PO947 hypothetical protein 13.31
M371 A7 H-PO949 conserved hypothetical secreted 16.61
protein
M371 B7. . .
. . .
factor Ile, 48.360
alpha subunit
M302 D7 H-S69022 myosin, light polypeptide 2, 18.26 3 1
ventricular
H5 H-S69272 cytoplasmic antiproteinase=38 41.47 50
kda intracellular serine proteinase
inhibitor [human, placenta,
mRNA, 1465 nt]
DI H-S72043 GIF=growth inhibitory factor 7.59 19
[human, brain, Genornic, 2015 nt]
M266 B3 H-S74221 cytokine lK factor 17.93 36.OkDa
DI H-S74445 cellular retinoic acid-binding 15.18 23
protein. . . small nuclear ribonucleoprotein, 13.97 17.OkDa
Sm D3
M311 D4 H-UI6660 enoyl-Coenzyme A hydratase-like 36.19 38
protein, peroxisomal
M302 H4 H-UI7074 cyclin-dependent kinase 6 18.59 29
inhibitor p 1 8
M306 A2 H-UI7195 A-kinase anchor protein I 00 72.05 100
[AKAPIOO*]
DI -UI7280 Steroidogenic acute regulatory 31.46 35
protein
M316 171 H-UI8291. . .
. . .
29.15 38.OkDa
factor TAF1132 mRNA, complete
cds
M424 H3 H-U22662 Human nuclear orphan receptor 49.28 49.OkDa
LXR-alpha mRNA, complete cds
M271 D2 H-U24074 killer cell inhibitory receptor 37.62 43
[KIR], Homo sapiens natural
killer-associated transcript 3
(NKAT3), complete cds.
. . .
30
gamma
M416 D3 H-U26403 Human receptor tyrosine kinase 25.19 30.OkDa
ligand LERK-7 precursor
(EPLG7) mRNA, complete cds
M317 E2 H-U27143 human protein kinase C inhibitor- 13.900
17.OkDa
I cDNA
E5 H-U28249 Human II kd protein mRNA, 12.32 12
complete cds
F4 H-U28386 Human nuclear localization 58.3 54
sequence receptor hSRP. . . phosphatase 2A, 56.65 55.OkDa
regulatory subunit B' alpha- I
El H-U37529 Human substance P beta-PPT-A 14.3 22
mRNA, complete cds
M305 H5 H-U37547 apoptosis inhibitor 68.09 64
M424 D5 H-U38480 Human retinoid X receptor- 51.04 61.OkDa
gamma mRNA, complete cds
M270 F4 H-U38810 Human mab-21 cell fate-
determining protein. . . mRNA
M298 E4 H-U39945 human adenylate kinase 2 (adk2) 26.3633 38.OkDa
mRNA
166-38 H-U40282 human integrin-finked kinase 55 49.68
(ILK) mRNA
169-65 H-U40343 human CDK inhibitor p I 9INK4d 1 8 18. 33

mRNA
E2 H-U40705 Homo sapiens telomeric repeat 48.4 52
binding factor (TRF I) mRNA,
complete cds
166-50 H-U40989. . . E2 H-U47677 Human transcription factor E2F 1
48.18 53.OkDa
(E2FI) gene, promoter and
m421 H I H-U48707 Human protein phosphatase- 1 18.92 36.OkDa
inhibitor mRNA, complete cds
M302 B7 H-U49070 peptidyl-prolyl isomerase PIN I 18.04 28.OkDa
C1 H-U49188 Human placenta (Diff33) mRNA, 54.45 70
complete cds
M485 H2. . .
. . .
46.97 60.OkDa
phosphodiesterase (PDE4Q
mRNA, 4C-426 isoform,
complete cds
M306 F3 H-U66867 ubiquitin-conjugating enzyme E21 17.49 28
[UBE2I]
M416 E2 H-U681 11 Human protein phosphatase 22.66 37.OkDa
inhibitor 2 (PPP I R2) gene
F2 H-U68382 Mannosidase, alpha B, lysosomal 35.64 36
G2 H-U69141 Glutaryl-Coenzyme A 48.29 56
dehydrogenase
B2 H-U70660 Human copper. . . (HAHI) mRNA, complete
cds
M297 B2 H-U71374 peroxisomal membrane protein 40.15 40.OkDa
(Pexl3p)
M306 A3 H-U75272 progastricsin [PGC] 42.79 49.OkDa
A2 H-U75285 Homo sapiens apoptosis inhibitor 15.73 25
survivin gene, complete cds
B2 H-U77456 Human nucleosome assembly 41.36 50
protein 2 mRNA, complete cds
C2 H-U78294 Homo sapiens 15S-lipoxygenase 74.47. . . and VIIIa)
M302 B3 H-XO2751 proto-oncogene N-ras 20.9 25.OkDa
D3 H-XO2812 Human mRNA for transforming 43.12 50
growth factor-beta (TGF-beta)
M302 CI H-XO3124 tissue inhibitor of 22.88 T6.OkDa
metalloproteinase I
M362 BI H-XO3342 ribosornal protein L32 14.96 24.OkDa
M235 A2 H-XO3484 human mRNA for raf oncogene 71.350 73.OkDa
M318. . .
. . .
basic protein, 23 kDa 22.44 30.OkDa
M318 GI H-X57025 insulin-like growth factor 1 16.94 1 8
M305 F5 H-X57348 protein kinase C inhibitor 27.39 35.OkDa
M236 D6 H-X57351 interferon-induced protein 1-813 14.63 24
H3 H-X57352 interferon-induced protein 1-8U 14.74 38
M305 B6 H-X58079 S- I 00. . . 49
E2 H-X59357 Epstein-Barr virus small RNA- 14.19 36
associated protein
M236 D4 H-X59417 macropain, iota subunit, THE 27.17 36
INTERACTION OF CALPONIN
WITH ACTIN INHIBITS
ACTOMYOSIN MG-ATPASE
ACTIVITY
M271 H4 H-X59618 ribonucleotide reductase, small 42.9 46
subunit
M250 G3 H-X59710 CAAT-box DNA-binding protein, 22.66 34
subunit B, CCAAT-BINDING
TRANSCRIPTION FACTOR
SUBUNIT A [Homo. . .
. . .
H+ transporting, 42.13 58.OkDa

subunit C, vacuolar
M236 C3 H-X69392 ribosomal protein L26 16.06 29
B3 H-X69532 H.sapiens gene for inter-alpha- 100.32 98
trypsin inhibitor heavy chain HI,
exons 1-3
M236 F5 H-X69654 ribosomal protein S26 12.76 18
M421 C8 H-X70218 Protein phosphatase 4 (formerly 33.88
X), catalytic subunit
M266. . .

M235 BI H-X72841 Human retinoblastoma-binding 46.86 52.OkDa
protein (RbAp46) mRNA,
complete cds, IEF 7442
(GB:X72841)
217-25 H-X73428 DNA-binding protein inhibitor 20 17.08
ID-3
M305 B5 H-X73459 signal recognition particle, 15.07 20
subunit 14
M250 D6 H-X73460 ribosomal protein L3, isoform 2, 44.44 50.OkDa
COMPONENT OF. . .
. . .
H-YO0291 Human hap mRNA encoding a 49.39 59.OkDa
DNA-binding hormone receptor
M386 HI H-YO0345 polyadenylate-binding protein 69.74 70.OkDa
M469 A2 H-YO0630 Plasminogen activator inhibitor, 45.76
46.OkDa
type II (arginine-serpin)
M305 El H-YO0711 lactate dehydrogenase B 36.85 38.OkDa
H2 H-YO0764 ubiquinol/cytochrome c reductase 10.12 33
hinge protein
F5 H-YO7848 H.sapiens. . .

=> d kwic 4

L23 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ABEN . . .
loss of one of these alleles in cancer cells due to loss of
heterozygosity (LOH) and (2) the
development of inhibitors with high specificity for the single
remaining alternative allele of the
essential gene retained by the tumor cell after LOH.. . .
ABFR . . . perte de l'un de ces alleles dans des cellules cancereuses, due a
la perte
d'heterozygotie (LOH); et (2) developper des inhibiteurs
presentant une specificite elevee pour
l'allele distinct restant du gene essentiel retenu par la cellule
tumorale apres LOH. Des categories. . .

DETD Specifically, this invention is concerned with target genes for drugs
that are useful
for treating such diseases by providing allele-specific
inhibition of essential cell
functions.
. . .
strategy for the development of anticancer agents having a high
therapeutic
232/116
index is described in Housman, International Application PCT/US/94 08473
and
Housman, INHIBITORS OF ALTERNATIVE ALLELES OF GENES
ENCODING PROTEINS VITAL FOR CELL VIABILITY OR CELL GROWTH
AS A BASIS FOR CANCER THERAPEUTIC AGENTS, U.S.. . . which undergo
loss of
heterozygosity in a cancer. Treatment of a cancer in an individual who

is
heterozygous with an allele specific inhibitor targeted to the single allele of an
essential gene which is present in a cancer will inhibit the growth of the cancer
cells. In contrast, the alternative allele present in non-cancerous cells (which have
not undergone loss of heterozygosity). . .
. . .
(3) identification of the absence of one of these alleles in cancer cells due to LOH and (4) development of specific inhibitors of the single
remaining allele of the essential gene retained by the cancer cell, but not the
alternative allele.

SUMMARY OF THE DWENTION
The utilization of inhibitors of alternative alleles, such as in the strategy described
in Housman, supra, requires the provision of suitable target genes in order to
identify such inhibitors and to implement corresponding diagnostic or therapeutic
methods. Thus, as described below, the present invention identifies useful groups
of genes which provide. . .

In each disease, the administration of such an inhibitor would have cytotoxic or
antiproliferative effects on the abnormally proliferating cells that exhibited LOH
and contained only the sensitive allele of the. . .

In addition, it was found that specific inhibitors of alternative alleles of an
essential gene would be useful in managing transplantation in instances where the
alleles in a donor bone marrow differ from the alleles in the recipient. For
example, administration of an inhibitor of an allele that was present in a donor
bone marrow but not the recipient could be used to treat graft-versus-host. . .

Alternatively, an inhibitor of an allele that is present in the recipient but not the
donor bone marrow could be used to enhance engraftment by preferentially creating space in the recipient bone marrow for the graft without inhibiting
proliferation of the engrafted donor marrow.

232/116
The term target gene refers to a gene where the gene, its RNA transcript, or its
protein product are specifically inhibited or potentially inhibited by a drug. In
references herein to genes or alleles, the term encoding refers to the entire gene
sequence, including both coding. . .
. . .
of alternative variances at a single variant site, or a combination of several different variances at different sites. In this invention, inhibitors targeted
to a specific allelic form or subset of the allelic forms of a gene can be targeted to

a specific variance. . .

. . .

dysplastic epithelium of
lung, breast, cervix, or other tissues. Drugs used in treating cancer
and other
non-cancer proliferative disorders commonly aim to inhibit the
proliferation of
cells and are commonly referred to as antiproliferative agents.

. . .

particular sequence
variance. Also preferably, these terms refer to loss of heterozygosity
of a
particular sequence variance that is recognized by an inhibitor
that will inhibit one
allele of the gene present in normal cells of the individual, but not an
alternative
allele.

. . .

the individual clones. The alleles subject to LOH may vary from one
clone to another. Therefore treatment of these conditions preferably
utilizes
inhibitors of at least two allelic forms. Thus, methods
relating to such disorders
can utilize alternative alleles of one gene and/or allelic. . .

. . .

of LOH in certain locations, for example segments of
chromosomes 7,8,10,11,13,16, and 18 in prostate cancer, administration
of an
allele-specific drug that inhibits one allele that is within
such a region, in a patient
who is heterozygous for alternative forms of the gene, would. . .

. . .

genes, and provides, as examples, specific genes within those categories
which are found to be suitable as targets for allele specific
inhibitors, in particular
for killing cancer cells or reducing the proliferation of cells in
cancer or noncancer
proliferative disorders. Thus, the present invention. . . more
variant
positions, indicates that the gene is a useful potential target gene in
this invention
for the identification of allele specific inhibitors and in
other aspects of the
invention.

. . .

those skilled in the art) identifying the gene and providing a known
sequence) which can be used for identifying allele specific
inhibitors and for use in
other aspects of this invention. Preferably the gene has the LOH
frequency and at
least one sequence variance. . .

. . .

vital for cell viability or growth, or essential
for cell survival and proliferation have the same meaning. A gene is
essential if
inhibition of the function of such a gene or gene product will
kill the cell or inhibit
its growth as determined by methods known in the art. Growth
inhibition can be
monitored as a reduction or preferably a cessation of cell
proliferation.

. . .

the affected gene, genetic disruption of the gene by homologous
recombination
or other methods in organisms ranging from yeast to mice,

inhibition of the gene
by antisense oligonucleotides or ribozymes, and identification of the target of
known cytotoxic, drugs and other inhibitors. As further discussed below, the
essentiality of a gene can depend on the conditions to which the cell is exposed.

. . .

entity is absent or present at low levels, the
gene product is essential. In another example, the administration of a drug that
inhibits one or more functions within the cell can cause other functions to be
essential that are not essential in the absence. . .

. . .

Identification of one or more sequence variances in
that gene and/or in the corresponding gene products allows screening or design of
such inhibitors for potential treatment.

. . .

sequence variance, and therefore of individuals heterozygous for such
variances, indicates that the gene can be used for the identification of inhibitors
targeting allelic forms of the gene which have a particular variance or variances
and in the other aspects of this invention.

. . .

gene is a potential target. The
target gene, its RNA transcript or protein product can then be used as targets for
allele-specific inhibitors for treating the proliferative disorder or other uses as
described in the aspects of this invention.

. . .

of the
population are heterozygous for that gene provides genes which are particularly
likely to be useful target genes for allele specific inhibition
in this invention.

. . .

or 50% of cases of such a disorder
indicates that the gene is useful as a potential target for identifying allele specific
inhibitors for the treatment of proliferative disorders and in other aspects of this
232/116
invention.

. . .

more preferably at least 30%, and most
preferably at least 40% are heterozygous in a specific population that may be
treated with inhibitors to treat cancer or other proliferative disorder in that
population. Once a specific variance is identified in a certain gene, the. . .

In the context of this invention, an alternative allele, or other reference to an
appropriate target for the inhibitors of this invention refers to a form of a gene
which differs in base sequence from at least,one other allele or. . . no
phenotypic effect on the physical condition of an individual having that variance
until the variance is targeted by an allele specific inhibitor

In connection with allele specific inhibitors and the methods of this invention, the terms allelic form or alternative form of the target gene or sequence variance within the. . . either or both of the gene or a product of that gene including the RNA transcript or protein product. Thus, a particular inhibitor may act in an allele specific manner (which will often be variance specific) at any of those levels and preferably the inhibitor is targeted to a particular sequence variance of the specific allelic form.

. . .

the classes described above in genes that are essential for cell survival or proliferation that can be the targets for allele-specific inhibitors for the treatment of cancer or noncancer proliferative disorders.

This invention provides inhibitors which are specific for at least one, but not all, allelic forms of a gene that encodes a gene product essential to cell growth or cell viability, for genes belonging to the specified categories of genes. The inhibitor may be active on the gene or gene product including the RNA transcript, protein product, or modifications thereof. Exposure to the inhibitor inhibits proliferation or kills cells which have undergone LOH of genes that are not inhibited by the drug and contain only an allelic form of the essential gene, its RNA transcript, or its protein product against which the inhibitor is targeted. Normal cells which contain two alternative alleles of the target genes, one of which is not inhibited by the specific inhibitor, are spared from the toxic effects of the inhibitor because the remaining activity of the allele which is not inhibited by the inhibitor is adequate to permit continued cell viability and growth. This differential effect of the inhibitor on cells with LOH of a targeted gene (e.g., a cancer cell) and normal cells accounts for the high therapeutic index of the inhibitors of this invention for the treatment of cancer or non-cancerous, proliferative disorders characterized by LOH. Toxicity of the inhibitor to normal cells is therefore low, compared to most currently available anticancer and antiproliferative agents.

. . .

indicated above and described in the Detailed Description of the Preferred Embodiments, in a first aspect the invention provides methods for identifying inhibitors potentially useful for treatment of a proliferative disorder, e.g., cancer. Such inhibitors are active on 232/116 specific allelic forms of target genes as identified herein. The method involves determining at least two allelic forms of such a gene encoding an

essential gene
product, and testing a potential allele specific inhibitor to determine whether the
potential inhibitor is active on, e.g., inhibits expression of, at least one of the
allelic forms, but not all of those forms. If the potential inhibitor inhibits only a
subset of the allefic forms of the particular essential gene, then it is an allele
specific inhibitor. Preferably the difference in activity of the inhibitor for
different allelic forms is between allelic forms which have a sequence variance at a
particular site.

In many, or even most, cases an allele specific inhibitor discriminates between two
allelic forms due to a particular single sequence variance between the allelic forms
of the target gene. For example,. . . not affect the cleavage. In the Detailed Description of the
Invention specific examples of proteins, small molecules, and oligonucleotides
providing allele specific inhibition based on single sequence variances are
described. Thus, in preferred embodiments an allele specific inhibitor
discriminates between two allelic forms by discriminating a single sequence
variance. As previously indicated, inhibitors can be targeted to either the nucleic
acid or a polypeptide (where a nucleotide change results in an amino acid change).

In particular embodiments, the allele specific inhibitor will recognize more than
one linked sequence variances within a specific allele.

An allele specific inhibitor or variance specific inhibitor is a drug or inhibitor
that inhibits the activity of one alternative allele of a gene to a greater degree than
at least one other alternative allele. The difference in activity is commonly
determined by the dose or level of a drug required to achieve a quantitative degree
232/116
of inhibition. A commonly used measure of activity is the IC50 or concentration
of the drug required to achieve a 50% reduction in the measured activity of the
target gene. Preferably an allele specific inhibitor will have at least twice the
activity on the target allelic form than on a non-target allelic form, more
preferably at least. . . most preferably at least 100 times. This can also
be expressed as the sensitivities of the different allelic forms to the inhibitor.
. . .
it is equivalent to state that the target allelic form is most preferably at least 100 times as sensitive to the inhibitor as a non-target allelic
form. The activity of an inhibitor can be measured either in vitro or in vivo, in

assay systems that reconstitute the in vivo system, or in systems incorporating selected elements of the complete biological system. For use in inhibiting cells containing only the target allelic form rather than cells containing at least one non-targeted allelic form, the difference in activity. . .

In a related aspect, the invention provides inhibitors potentially useful for tumor, e.g. . cancer treatment, or treatment of other proliferative disorders. Such inhibitors are active on a specific allele of a gene which has at least two different alleles encoding an essential gene product in one of the target gene categories above. Such inhibitors can, for example, be identified by the above screemng methods.

In a related aspect, the invention provides methods for producing inhibitors active on such specific allelic forms of belonging to one of the above categories genes by 232/116 identifying a gene encoding an essential. . . product which has alternative allelic forms in a non-tumor cell and which undergoes LOH in a tumor cell, screening to identify an inhibitor which is active on at least one but less than all of the alleles of the gene, and synthesizing the inhibitor in an amount sufficient to produce a therapeutic effect when administered to a patient suffering from a tumor in which tumor cells have only the allele on which the inhibitor is active.

In the context of this invention, the term active on an allefic form or allele specific inhibitor or specific for an allelic form indicates that the relevant inhibitor inhibits an allele having a particular sequence to a greater extent (preferably > 2x) than an allele having a sequence which differs in a particular manner. Thus, for alleles for which a particular base position is identified, the inhibitor has a higher degree of inhibition when a certain base is in the specified position then when at least one different base is in that position. This. . . means that for substitution at a particular base position, at least two of the possible allelic forms differ in sensitivity to an inhibitor. Usually, however, for a specific sequence variance site, the site will be occupied by one of only two bases.

Further, if an inhibitor acts at the polypeptide level, and any of three bases may be present at a particular position in a coding sequence but only one of the substitutions results in an amino acid change, then the activity of the inhibitor

would be expected to be the same for the two forms producing the same amino
acid sequence but different for the form. . .

The term less active indicates that the inhibitor will inhibit growth of or kill a
cell containing only the allelic form of a gene on which the inhibitor is more active
at concentrations at which it does not significantly inhibit the growth of or kill a
cell containing only an allelic form on which the inhibitor is less active.

232/116
The term drug or inhibitor refers to a compound or molecule which, when
brought into contact with a gene, its RNA transcript, or its gene product which the
compound inhibits, reduces the rate of a cellular process, reduces the level of a
cellular constituent, or reduces the level of activity of. . . the term to those skilled in the art and not limiting. Thus, the term generally indicates that a compound has an inhibitory effect on a cell or process,
as understood by those skilled in the art. Examples of inhibitory effects are a
reduction in expression of a gene product, reduction in the rate of catalytic activity
of an enzyme, and reduction. . . formation or the amount of an essential
cellular component. The blocking or reduction need not be complete, in most
cases, for the inhibitor to have useful activity. Thus, in the present invention,
inhibitors are targeted to genes, their RNA transcript, or their protein product
that are essential for cell viability or proliferation. Such inhibitors would have the
effect of inhibiting essential functions, leading to loss of cell viability or inhibition
of cell proliferation. In preferred embodiments, such inhibitors cause cell death or
stop cell proliferation. In preferred embodiments of this invention, inhibitors
specifically include a molecule or compound capable of inhibiting one or more,
but not all, alleles of genes, their RNA transcript, or their protein product that are
essential for cell survival or proliferation. The terms inhibitor of a gene or
inhibitor of an allele as used herein include inhibitors acting on the level of the
gene, its gene product, its RNA transcript, its protein product, or modifications
thereof and is explicitly not limited to those inhibitors or drugs that work on the
gene sequence itself.

Several types of inhibitors are generally recognized in the art. A competitive
inhibitor is one that binds to the same site on the gene, its RNA transcript or gene
product as a natural substrate. . . is required for the action of the gene
or gene product, and competitively prevents the binding of that

substrate. An
232/116
66 allosteric inhibitor is one that binds to a gene or gene product and alters the
activity of the gene or gene product without preventing binding of a substrate or
cofactor. Inhibition can also involve reducing the amount of the gene, RNA
transcript, or its protein product, and thus the total amount of activity from the
gene in the cell. Such inhibition can occur by action at any of a large number of
different process points, including for example by inhibiting transcription or
translation, or by inducing the elimination of the gene, its RNA transcript, or its
protein product where elimination may involve. . . of the target or egress or export from the compartment in which it is active and the process of
excretion or export. Inhibition can also be achieved by modifying the structure of
the target, interfering with secondary modifications, or interfering with cofactors
or other ancillary components which are required for its activity. Inhibitors can be
comprised of small molecules or polymeric organic compounds including oligopeptides or oligonucleotides.

The term active on a gene or targeted to a gene indicates that an inhibitor
exerts its inhibitory effect in a manner which is preferentially linked with the
characteristic properties of a gene, its RNA transcript or its gene. . . RNA with other cellular constituents (RNA, protein, cofactors, substrates, etc.)
required for activity. Thus, in general these terms indicate that the inhibitor acts
on the gene, its RNA transcript, its protein product, its gene product, or
modifications thereof, or on a reaction or reaction. . .

. . .
from one of the
above categories has undergone loss of heterozygosity. The method involves
administering a therapeutic amount of an allele specific inhibitor of such an
essential gene to a patient whose normal somatic cells are heterozygous for that
gene but whose tumor cells contain only a single allelic form of the gene. The
inhibitor is active on the specific allele of the gene present in the tumor cells.

. . .
cancer. The method involves administering to a patient having a precancerous condition or an early stage cancer or cancers an allele specific
inhibitor targeted to an allele of an essential gene for which the normal somatic
cells of the patient are heterozygous and which. . . the precancerous condition are not clonal from a single cell, the method involves
subsequently administering to the patient a second allele specific inhibitor in an
amount sufficient to inhibit and preferably kill cells with LOH in which an allele

not targeted by the first inhibitor is the only remaining allele of the gene. In most cases, the second allele specific inhibitor will target the alternative allele of the gene targeted by the first inhibitor. However, the second inhibitor can also target an allele of a second essential gene which has undergone LOH. The second gene may have undergone LOH in. . . affected the first gene due to their proximity on a chromosome, though this is not essential. Additionally, in other cases, allele specific inhibition of one of the alleles of each of 3, 4, or even
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more target genes can be utilized in a serial. . . genes need not be tightly linked so that LOH of the various genes does not necessarily occur together. By using the serial inhibition of an allele of each of the target genes, it is possible to inhibit and preferably kill the full population of precancerous cells in which LOH has occurred. Thus, the net effect is essentially the same as if allele specific inhibitors of each of the two alternative alleles of one essential gene had been used.

In the context of the administration of multiple allele specific inhibitors, the terms serial or subsequently indicates that the administration of two or more inhibitors is sufficiently temporally separated so that normal somatic cells remain functional and are therefore able to survive and/or proliferate. Those skilled. . . that the required time will depend on various factors, such as clearance rate, type and extent of the effect of an inhibitor on normal cells, and additive cellular toxicity, and that appropriate timing can be routinely determined for particular selections of compounds.

In another related aspect, the invention provides a method for identifying a potential patient for treatment with an inhibitor active on a specific allele of an essential gene from one of the above categories. The method involves identifying a patient having. . . the neoplastic cells contain only a single allele of the gene, then the patient is a potential patient for treatment with the inhibitor.

With respect to identifying patients with precancerous or oligoclonal proliferative
232/116
diseases characterized by LOH, and selecting appropriate allele or variance-specific inhibitors for such patients, in some cases it may not be practical to obtain samples of all proliferative lesions for LOH assays... . . aorta cannot routinely be sampled by biopsy, and dysplastic lesions in the cervix, colon, or bronchus can be multifocal. Therefore, allele specific inhibitors can be selected for such conditions based on previously established

patterns of LOH for the condition, and on specific testing for. . .
. . .
most preferably 100%. However, it is not necessary that 100% of lesions show LOH for a successful treatment by allele specific inhibitors because 2,3,4, or even more inhibitors can be used in a combined approach to target an ever higher fraction of lesions, and because substantial therapeutic benefit may be achieved by inhibiting the proliferation of less than 100% of lesions.

In another aspect, the invention provides a method for identifying a potential patient undergoing transplantation for treatment with an inhibitor active on a specific allele of an essential gene from one of the above categories. The method involves identifying a patient undergoing. . .
. . .
related aspect, the invention provides a method for treating graft versus host disease in allogenic transplantation in which an allele specific inhibitor is used to inhibit proliferation of donor cells, e.g. . to inhibit stimulation of the donor immune system. In preferred embodiments, the allele specific inhibitor is selected by identifying alternative variances or allelic forms of an essential gene that are present in the donor tissues but not the recipient. Therapy with a variance or allele specific inhibitor or inhibitors that recognizes both alleles of the essential gene that are present in the donor, but not both alleles of the same. .
.
. . .
another aspect, the invention provides a method for enhancing engraftment of an allogenic bone marrow transplant in which an allele specific inhibitor is used to kill or suppress the patient's own bone marrow, providing space for engraftment of the donor cells within the marrow cavity. In preferred embodiments, the allele specific inhibitor is selected by identifying alternative forms of an essential gene that are present in the recipient but not the donor marrow. Therapy with an allele specific (generally a variance specific) inhibitor that recognizes both forms of the essential gene that are present in the recipient, but not both forms of the same gene. . .

Allele specific inhibitors can be used to treat or prevent chimerism by selectively killing or suppressing proliferation of the patient's own cells without toxicity. . .
. . .
aspect, the invention provides a method for treating cancer in a patient receiving allogenic or autologous transplantation in which an allele specific inhibitor is used to kill or inhibit the growth of cancer cells without toxicity to the transplanted marrow. In one embodiment, in an autologous, transplantation the

allele specific inhibitor is selected to recognize one alternative allele of an essential gene remaining in the cancer cell due to LOH in patients. . . therapy of cancer without suppression of the transplanted marrow. In an alternative embodiment, in an allogenic transplantation, therapy with an allele specific inhibitor that recognizes the one form of the essential gene that is present in cancer cells due to LOH in the recipient,. . . tissue for selective reimplantation. The present invention provides for an improved method for purging bone marrow of malignant cells using allele specific inhibitors of essential genes. The method involves identifying an essential gene with only one variant form remaining in the cancer cells due. . . The patient's bone marrow is then cultivated ex vivo using methods known in the art in the presence of an allele specific inhibitor that inhibits the allele that is present in the cancer cells, but not the alternative allele that is present in the heterozygous normal bone. . .

In another aspect, the invention provides a method for inhibiting growth of or killing a cell containing only one allelic form of a gene by contacting the cell with an inhibitor active on that allelic form. The gene has at least two sequence variants in a population, and belongs to one of the categories of essential genes described below. The inhibitor is less active on at least one other allelic form of the gene.

In preferred embodiments of the above aspects in which an allele specific inhibitor is used to inhibit a cell or to treat a patient, a plurality of different inhibitors may be used. Preferably different inhibitors target a plurality of different variances in a single target gene, or target variances in different target genes, or both. In particular embodiments a plurality of inhibitors is used simultaneously, in others there is serial administration using different inhibitors or different sets of inhibitors in separate administrations, which may be performed as a single set of administrations in which each set of inhibitors is administered once, or in multiple serial administrations in which each set of inhibitors is administered more than once. Such use of multiple inhibitors provides enhanced inhibition, which preferably includes killing, of the targeted cells. In addition, allele specific inhibitors as described can be used in conjunction with other treatments for diseases and conditions, including in conjunction with other chemotherapeutic agents such. . .

In a related aspect, an allele specific inhibitor can be used in conjunction with a conventional antiproliferative or chemotherapeutic agent or therapy, such therapies including radiation, immunotherapy, or surgery. In. . . . with the above aspects, in a further aspect the invention provides a pharmaceutical composition which includes at least one allele specific inhibitor.

In preferred embodiments the composition includes at least one allele specific inhibitor and a pharmaceutically acceptable carrier. Such carriers are known in the art and some commonly used carriers are described in the Detailed Description below. Also in preferred embodiments the composition includes two, three, or more allele specific inhibitors, and may also include a pharmaceutically acceptable carrier. In other preferred embodiments, the composition includes at least one allele specific inhibitor and another antineoplastic agent, which need not be an allele specific inhibitor. The embodiments of this aspect may also optionally include diluents and /or other components as are commonly used in pharmaceutical compositions or formulations. In embodiments having a plurality of allele specific inhibitors, the inhibitors may target a plurality of different variances of a single target essential gene, or may target sequence variances of a plurality of. . .

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In accord with the use of pharmaceutical compositions, the present invention also provides a packaged pharmaceutical composition comprising an allele specific inhibitor as described above, bearing a Food and Drug Administration use indication for administration to a patient suffering from a cancer or. . .

Thus, similar to the above, the invention provides a method for identifying an inhibitor potentially useful for treatment of cancer or other proliferative disorder.

The inhibitor is active on a conditionally essential gene, and the gene is subject to loss of heterozygosity in a cancer. The method. . . least two alleles of a said gene which differ at at least one sequence variance site and testing a potential allele specific inhibitor to determine whether the potential inhibitor is active on at least one but less than all of the identified alleles. If the potential inhibitor inhibits expression of at least one but less than all of the alleles or reduces the level of activity of a product of at least one but less than all of the alleles, this indicates that the potential allele specific inhibitor is, in fact such an allele-specific

inhibitor inhibitor.

Similar to other types of target genes described above, the invention provides
inhibitors, methods for producing inhibitors,
pharmaceutical compositions, methods
for identifying potential patients, probes, and primers which target or recognize
alleles of a conditionally essential gene or utilize inhibitors
which target such genes.

. . .
also provides methods for preventing the development of cancer,
methods for treating a patient suffering from a cancer, and methods for inhibiting
growth of a cells as described above except that the targeted cells are subjected to an
altered condition such that the gene. . .

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In still another aspect, not requiring the use of allele specific inhibitors, but still
utilizing information about sequence variance or allelic differences between normal
somatic cells and cancer cells in a patient, the invention. . .

. . .
above aspects, a conventional therapy acts on a protein
or other molecular target in the same pathway as the allele specific inhibitor. As an
example, the antineoplastic drug hydroxyurea, which inhibits ribonucleotide
reductase (RR), can be used in conjunction with an allele specific inhibitor of RR
subunit MI or M2 or another gene that encodes a product important in nucleotide
synthesis. Similarly, the antiproliferative drug methotrexate inhibits the enzyme
dihydrofolate reductase (DHFR), and can be used with allele specific inhibitors of
DHFR that would result in a differential methotrexate effect on cancer tissues
compared to normal proliferating tissues. Alternatively, methotrexate can be used
with allele specific inhibitors of other genes important in folate metabolism to
achieve an enhanced cancer cell specificity for methotrexate. Similarly, the
anticancer drug 5-fluorouracil and related compounds can be administered together
with an allele specific inhibitor of thymidylate synthase (TS) in a patient
heterozygous for TS and with LOH at the TS gene in proliferating cells, e.g., cancer
cells. Alternatively, an allele specific inhibitor of 5-FU degradation or metabolism
can be administered with 5-FU. For example, the enzyme dihydropyrimidine
dehydrogenase, which catalyzes the first and rate. . .

. . .
LOH in one or more tumors or other
proliferative disorders. Genes having these characteristics can then be used for
identifying allele specific inhibitors and evaluated for use in the other methods of
this invention. Such procedures are routine, as is shown by the Detailed
Description. . .

In preferred embodiments of the above methods and inhibitors involving particular target genes or classes or categories of genes, the inhibitor or potential inhibitor is a ribozyme which is designed to specifically cleave a particular target allelic form of a gene (i.e., a nucleotide sequence such. . .

Similarly, in preferred embodiments the inhibitor or potential inhibitor is an oligonucleotide, e.g, an antisense oligonucleotide, preferably at least partially an oligodeoxyribonucleotide. The antisense oligonucleotide is complementary to a sequence which includes. . .

Thus, derivatives of nucleic acid inhibitors include modified nucleic acid molecules which may contain one or more of: one or more nucleotide analogs, including modifications in the sugar. . .

Similarly, in preferred embodiments the inhibitor or potential inhibitor is an antibody, preferably a monoclonal antibody, which may be complexed or conjugated with one or more other components, or a fragment. . .

An inhibitor may also be an oligopeptide or oligopeptide derivative. Such peptides may be natural or synthetic amino acid sequences, and may have modifications. . .

In other embodiments, the inhibitor is a small molecule, for example, a molecule of one of the structural types used for conventional anticancer chemotherapy.

. . .

region undergoes LOH at frequencies similar to the marker. Such gene identification thus further identifies particular cancers which can potentially be treated with inhibitors targeting sequence variances in those essential genes.

. . .

LOH for other such disorders and cancers, and can further readily identify essential genes which are potential targets for variance specific inhibition and the treatment of the corresponding condition and in other aspects of this invention.

. . .

72 hours after transfection with antisense oligonucleotides. Anti-ras is an oligonucleotide known to have antiproliferative effects against T24 cells. This oligonucleotide exhibits inhibition comparable to the anti-RPA70 oligonucleotide.

. . .

is two graphs showing that the proliferation of two cell lines homozygous for different variant forms of the RPA70 gene is inhibited to a greater degree by matched oligonucleotides than by oligorners having a single base mismatch. Cell proliferation was measured by BrdU incorporation. . .

232/116
Fig. 13 is a graph showing Inhibition of BrdU incorporation in A549 cells by
antisense oligonucleotides against the RPA 70 gene. Cells were transfected, as
described previously, with a. . .

Fig. 20 is a graph showing inhibition of mutant ras using antisense
oligonucleotides specific for the mutant form, based on information available in
Schwab et al., 1994, PNAS 91:10460. . .

. . .
and
the variant sequences within these genes, have utility for the therapy of cancer and
other disorders through the discovery of variance-specific inhibitors.

Gene targets for a variance-specific inhibition strategy in this invention satisfy three
criteria.

A large number of references have identified essential genes which constitute actual
or potential targets for allele specific inhibition. The identification of essential genes
can be approached in various ways.

. . .
carbohydrates, lipids, organic ions, and inorganic ions, or cytoskeletal
elements. The loss of homeostasis often results in cell death or apoptosis or
inhibition of cell proliferation. Homeostasis in a living cell is dynamic, and
programed changes in homeostasis are required through the life cycle. .
.
. . .
those genes whose products are required for maintaining this homeostasis conducive to cell growth and survival are targets for anti-neoplastic
e.g., anti-cancer, inhibitors as described in the methods herein. For example, many
genes are involved in synthetic functions, allowing the cells to produce essential
cellular. . .

. . .
affecting the gene in a neoplastic disorder, establishes that the gene is a target gene potentially useful for identifying allele specific inhibitors
and for other aspects of the invention. In addition, as described, target genes are
useftil in embodiments of certain aspects of the. . .

. . .
(Type I Beta) L25441
GGTI3 (Geranylgeranyltransferase) Y08201
Geranylgeranyltransferase (Type 11 Beta-Subunit) X98001
3.5 Genes required for regulation of levels of organic ions
Gdp Dissociation Inhibitors
GDI Alpha (RAB GDP Dissociation Inhibitor Alpha) D45021
Rab Gdp (RAB GDP Dissociation Inhibitor Alpha) D13988
4) Genes Required to Maintain Cellular Proteins at Levels Compatible with Cell Growth or Survival
Polypeptide precursor biosynthesis
Amino acid biosynthesis and. . . processing peptidase alpha subunit)

D50913
MMP7 X07819
Proteasorne Beta 6 D29012
Proteasome Beta 7 D38048
Proteasorne C13 U 1 7496
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Proteasome C2 D00759
Proteasome C7-1 D26599
Proteasome inhibitor hPI31 subunit D88378
Proteasome P I 12 D44466
Proteasome P27 ABOO3177
Proteasome P55 ABOO3103
Ubiquitin System
Enzyme E2-17 Kd(Cyclin-selective ubiquitin carrier protein) U73379
ISOT-3(Ubiquitin carboxyl-terminal hydrolase. . .
. . .
Cell Shape and Motility at Levels
Compatible with Cell Growth or Survival
Cell structure genes (Cytoskeleton)
Actin X04098
Beta-Centractin X82207
Capping Protein Alpha U03851
CFL I (Cofilin, Non-Muscle Isoform) X95404
Desmin J03191
Dystrophin U26743
Gelsolin X04412
hOGG I (Myosin Light Chain Kinase) ABOO0410
IC Heavy Chain U31089
Itga2 (Integrin, Alpha 2 (CD49B, alpha. . .

Therapy with inhibitors of conditionally essential genes involves administration of the inhibitor together with a chemical or physical elements that causes the target gene to be essential for cell survival or proliferation. The use of allele specific inhibitors in the current invention allows specific killing of cancer cells with such chemical or physical agent since the gene function that is essential for the survival of cells (in the presence of the chemical or physical agent) is inhibited in the cancer cell but not in the normal cell.

. . .
are responsible for maintaining cell survival or proliferation in the presence of a drug or biological material. For example, a drug that inhibits one pathway for maintaining the level of a cellular constituent within levels required for cell survival or proliferation may make alternative pathways essential. In a specific embodiment, the inhibition of a synthetic pathway for a cellular constituent may make alternative synthetic pathways essential for cell survival or proliferation. Alternatively, a. . . from the cell essential for continued survival or proliferation. It will be evident to those skilled in the art that anything which inhibits the ability of a cell to survive in the presence of a specific drug that is designed to be cytostatic or cytotoxic, will sensitize that cell to the effects of the drug. A chemosensitizing agent is one that inhibits a function

in the cell that is
conditionally essential due to the administration of a chemotherapeutic drug.

. . .

in DNA repair may be essential that are not essential in the absence of the
external physical force. An agent that inhibits functions in the cell that are essential
due to the adminitration of ionizing radition would be termed a radiosensitizing
agent.

. . .

physical factors, determining whether
such genes are subject to loss of heterozygosity, identifying alternative alleles in
these genes and developing allele specific inhibitors of alternative forins of the gene.

The administration of such an inhibitor to a patient who has two alternative forms of
the gene in normal cells but only one in the cancer cell. . .

Thiopurinemethyltransferase (GenBankU12387)
e. Inactivation or transformation of other drugs including, but not limited to, purine analogs, folate analogs, topoisomerase inhibitors
and tubulin acting drugs via specific enzymatic modification.

I-kappa B alpha (GenBank M69043)
Increased expression of exogenous I kappa B-alpha, an inhibitor of
NF-kappa B, increases cell sensitivity to ionizing radiation. Thus is conditionally essential for cells exposed to ionizing radiation.

. . .

affect the gene sequence, RNA
sequence, or protein sequence of the gene or its gene products, which would
facilitate the design of inhibitors of the protein product, or be a base difference
anywhere within the genomic DNA sequence, including the promoter or intron
regions. Such DNA sequence variance can be exploited to design inhibitors of
transcription or translation which distinguish between two allefic forms of the
targeted gene. Sequence variants that do not alter protein sequence. .

. . .

genes located in regions which are
characteristically associated with LOH for a particular cancer, or other tumor are
particularly advantageous targets for inhibitors useful for treatment of that cancer or
tumor because such genes will also characteristically undergo LOH at high
frequency. The fact that. . . LOH occurs before the clonal expansion of cancers
in precancerous, abnormally proliferating tissue is potentially useful for preventing
cancer with allele specific inhibitors of essential genes.

. . .

disorder will indicate that the allele specific
treatment would be appropriate for the disorder. For the application of the general
allele specific inhibition strategy to such conditions (e.g..

selection of target gene
and variance, identification of inhibitors, selection of
composition and
administration method appropriate for the condition and the
inhibitor), the cells
associated with the condition correspond with the tumor, e.g., cancer
cells, for the
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methods described in the Summary above.

. . .
at least one marker. This does not
necessarily represent the maximum fraction of plaques which could
potentially be
treated with allele specific inhibitors because the study did
not attempt to determine
the sites of maximum LOH on each arm. LOH which is partial arm. . .

. . .
allele of the essential
gene is lost from the patient's cancer cells, the retained allele can be
targeted with an
allele specific inhibitor. Such an inhibitor will
kill, or reduce or prevent the growth
of cancer cells by abolishing the fimction of an essential gene. Normal
cells, which
retain both uninhibited and inhibited alleles, will survive or
grow due to the
expression of the uninhibited allele. This is clearly indicated because
tumor cells
having only one allelic form (after LOH) thrive, thus, normal cells will
also
function normally with one of two allelic forms inhibited.

. . .
neuroectodermal
tumor
Rhabdomyosarcoma
17q Breast carcinoma
Neurofibroma: N171
22q Acoustic neurinoma
1 8 Renal cell carcinoma Colorectal carcinoma
18q Breast carcinoma Ependymoma
Colorectal carcinoma Meningioma
Neurofibroma
V. Use of variance-specific inhibitors of essential genes to
treat non-malignant,
proliferative conditions.

. . .
will differ, with, for example, allele A
of a hypothetical essential gene lost in some plaques and allele A' in
others. An inhibitor of allele A would be expected to kill (or
arrest
growth of) only about half of all the plaques with allele. . .
plaques hernizygous for A. To kill the other
half of the plaques with allele loss at the target locus would require
an
inhibitor of A'. Simultaneous use of inhibitors of A
and A' would be
highly toxic to diploid normal cells. However serial use of an
inhibitor
directed to allele A followed by an inhibitor directed to A'
(perhaps
repeating treatment for several cycles, or even indefinitely) would
alternately abolish essential gene function in one half of all haploid
plaque
cells and then the other half, leading eventually to death or sustained
inhibition of proliferation of all plaque cells. Normal cells

would retain
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50% gene function in the presence of inhibitor (either from allele A or
allele A'). This therapeutic approach is applicable to the eradication of
any clonal proliferation of cells in. . .
. . .
surgically removed, LOH has been well described. As
with atherosclerotic plaques, these tumors are frequently multifocal and
therefore the approach of serial inhibition of allele A followed by
inhibition of allele A' would alternately abolish essential gene function in
one half of all haploid tumor cells and then the other half, leading
eventually to death or sustained inhibition of proliferation of all tumor
cells.
. . .
one allelic form in individuals whose normal somatic cells are
heterozygous for the particular essential gene. The essential gene can therefore
be inhibited by an allele specific inhibitor, i.e., a variance specific inhibitor. In
some conditions, however, multiple, independently arising lesions in an
individual are subjected to LOH in a disease or condition, e.g., in. .
.

It was determined that such conditions can be treated using allele specific
inhibitors despite the presence of both alleles in cells related to the condition.

There are two strategies for such therapy. The first is to serially administer
different inhibitors targeted to the different allelic forms of the target gene. This
can be accomplished by using inhibitors which target the alternative sequence
variants of one sequence variance site. Simultaneous administration of inhibitors
of both allefic forms of an essential gene would inhibit the cells which have
undergone LOH at that gene, but would also inhibit the normal heterozygous cells
of the individual. This treatment would inhibit essential ftinctions in normal cells
as well as cancer cells and have no advantage over the administration of
conventional antiproliferative drugs, many of which are inhibitors of known
essential functions. In contrast, administration of the first inhibitor targets the
subset of cells which have only the first allelic form of an essential gene. As
described for the general strategy, this inhibitor will not significantly affect the
growth or survival of the normal heterozygous somatic cells. This first
administration is followed by administration of a second inhibitor; the second
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inhibitor targets the cells which contain only the second allelic form of the gene,
and again does not significantly affect the normal. . . will
be useful. Similarly, recurring, or even indefinitely continued alternating

administrations will provide useful treatment. Likewise, these methods can
incorporate the use of inhibitors targeted to specific alleles of a plurality, e.g., 2,
3, 4, or more different target genes.

. . .

in non-malignant diseases are not
clonal, there may be systematic loss of one parental chromosome allowing
effective therapy with only one variance-specific inhibitor. This would occur, for
example, if there were an inherited or early embryonic mutation within a tumor
suppressor gene on one parental. . . of the corresponding normal tumor suppressor
gene on the other parental chromosome would lead to abnormal proliferation. In
such cases a variance-specific inhibitor of an essential gene that was closely
linked to the normal tumor suppressor gene would preferentially kill cells in the
proliferating lesion.

VI. Characteristics of allele-specific inhibitors

As indicated above allele specific inhibitors or allele specific anti-neoplastic
agents represent a new approach to tumor therapy because they are lethal or
significantly inhibit the growth only of tumor cells. The advantages of this
approach include, first, lack of toxicity to the normal cells of. . . a therapeutic index greater than that of conventional tumor, e.g., cancer
chemotherapy drugs, and second, it is not necessary that the inhibitors be targeted
specifically to the tumor cells, as they can be administered systemically. As also
described above, usually an allele specific inhibitor is specific for a single
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sequence variance of an essential gene, though in some cases the inhibitor utilizes
the joint effects of two or more sequence variances on a particular allele.

It is not necessary for the allele specific inhibitor to have absolute specificity.

. . .

of a gene product
encoded by the essential gene will often show a reduction in gene activity when
they take up the inhibitors of this invention, but should remain viable due to the
activity of the protein encoded by the uninhibited allele. On the other hand,
tumor cells expressing only one allele due to LOH, will respond to the inhibitors
of this invention which are specifically directed to the remaining allele, with a
greater reduction in gene activity. Growth of tumor cells exposed to the inhibitors of this invention will be inhibited due
to the suppression of either the
synthesis or the biological activity of the essential gene product.

. . .

only two allelic forms in any given individual, the
gene can have more than two allelic forms in a human population.

Accordingly, inhibitors can be targeted to any of the alleles in the population. A particular inhibitor will generally be targeted to a subset of the allelic forms; the members of the subset will have a particular sequence variance which provides the specific targeting. In some cases, however, the inhibitor will jointly target two, or possibly more sequence variances.

Once two or more alleles are identified for a target essential gene, inhibitors of high specificity for an allele can be designed or identified empirically. Inhibitors that can be used in the present invention will depend on whether allelic variation at a target locus affects the amino acid . . . the mRNA sequence, or the DNA in intron and promoter regions. If there is variation at the protein level, then classes of inhibitors would include low molecular weight drugs, oligopeptides and their derivatives, and antibodies, including modified or partial
232/116
antibody fragments or derivatives. For mRNA or DNA sequence variance the main class of inhibitors are complementary oligonucleotides and their derivatives and catalytic RNA molecules such as ribozymes, including modified ribozymes.

The generation of inhibitors of this invention can be accomplished by a number of methods. The preferred method for the generation of specific inhibitors of the targeted allelic gene product uses computer modeling of both the target protein and the specific inhibitor. Other methods include screening compound libraries or microorganism broths, empirical screening of libraries of peptides displayed on bacteriophage, and various immunological approaches.

Further, in the treatment of cancer patients, a therapeutic strategy includes using more than one inhibitor of this invention to inhibit more than one target. In this manner, inhibitors directed to different proteins essential to cell growth can be targeted and inhibited simultaneously. The advantage of this approach is to increase the specificity of the inhibition of proliferation of cancer cells, while at the same time maintaining a low incidence of side effects.

. . .
structure of the alternate allelic forms of the proteins, determinants can be identified which distinguish the allelic forms. Novel low molecular weight inhibitors or oligopeptides can then be designed for selective binding to these determinants and consequent allele-specific inhibition. Descriptions of targeted drug design can be found, for example, in I. Kuntz, Structure-Based Strategies

for Drug Design and Discovery, Science 257:1078-1082. . . have been described in Piper et al., Studies Aided by Molecular Graphics of Effects of Structural Modifications on the Binding of Antifolate Inhibitors to Human Dihydrofolate Reductase, Proc Am. Assoc. Cancer Res. Annual Meeting 33:412 (1992); Hibert et al., Receptor 3D-Models and Drug Design, Therapie. . .

Low molecular weight inhibitors specific for each allelic protein form can be predicted by molecular modeling and synthesized by standard organic chemistry techniques. Computer modeling can. . .

The inhibitors of this invention can be identified by selecting those compounds that selectively inhibit the growth of cells expressing one allelic form of a gene, but do not inhibit the activity of the A allelic form.

B. Small Molecule Inhibitors
232/116
Low molecular weight inhibitors can be identified and generated by at least one of the following methods; (1) screening of small organic molecules present in microorganism. . .

Inhibition of protein function following differential binding. Several mechanisms of inhibition are possible including.

competitive inhibition of active sites or critical allosteric sites,
allosteric inhibition of protein function,
altering compartmentalization or stability, and
inhibition of quaternary associations.

. . .
compounds that interact with particular features of a polypeptide or protein or protein complex, There are clear precedents for developing drugs, i.e., inhibitors, that are variance-specific including drugs that are allosteric inhibitors of protein functions. Several lines of experimental evidence demonstrate that small molecule variance specific
232/116
inhibitors can be designed and constructed for particular targets. Specifically.

Allosteric (noncompetitive) inhibition of protein function may be induced by binding ligands to many different surfaces of a protein. Ligands can cause allosteric inhibition by disturbing secondary, tertiary or quaternary (subunit-subunit) interactions of a protein. There is ample evidence that such effects can e induced by. . .

232/116
Competitive inhibitors can exert variance-specific effects by exhibiting differential affinities for variant active sites, thereby interfering

with
binding of the substrate or critical allosteric. . .

Competitive inhibitors may bind with equal affinity for the
active site but
exerting different effects on the structure or function of the variant
domain.

Allosteric inhibitors can exert variance-specific effects by
binding
differentially to variant forms of the active domain and distorting the
structure or function of the. . .
. . .
model the topology and surface chemistry of the target
in detail. These data are useful in optimizing the binding specificity
or
allosteric inhibitory function of the product through a series
of iterative
steps once a prototype binding ligand is identified. Structural modeling
of
the target. . .

Sites of allosteric inhibition
Most drug development focuses on competitive inhibitors of
protein action rather
than noncompetitive, allosteric inhibitors. There is no a
priori advantage to a
competitive versus allosteric inhibitor except for the fact
that medicinal chemistry
often begins with candidate molecules derived from natural substrates or
cofactors. There are, in fact, conceptual advantages to allosteric
inhibitors since
each protein may contain multiple allosteric sites, and allosteric
inhibitors may be
effective at lower concentrations (e.g. those equivalent to the
substrate) since
there is no need to compete with the substrate. . .

Detailed crystallographic and other structural studies of a variety of
enzymes
show that the mechanism of allosteric inhibition commonly
involves
conforinational changes (e.g. domain movements) far from the site of
contact
with the allosteric regulator. These data illustrate the cooperativity.
. .
. . .
several well-characterized proteins. Another is to examine the
distribution of epitopes for antibodies that bind to the surface of a
protein and
inhibit its function. Analyses of these types show that
allosteric sites are widely
dispersed within proteins and may comprise the majority of. . .
. . .
Three HIV-1 RT structures have been published, including
complexes with double stranded DNA at 3.0 A resolution and with the non-
nucleoside inhibitors nevirapine (at 3.5A) and -APA (at 2.8A).

Two classes of HIV-1 RT inhibitors have been developed. The
first class
comprises nucleoside analogues including AZT, ddI and ddC. The second
class
comprises non-nucleoside analogues belonging to. . . 5 shows the
location of selected mutations within HIV-1
RT that cause resistance to nucleoside analogues as well as the

mechanism of
inhibition postulated from physical-chemical experiments and structural data; the
list is not comprehensive.

Table 4
232/116
Location and postulated mechanism of amino acid substitutions which confer
resistance to nucleoside analog inhibitors. trp266X - multiple substitutions.

analog resistance arises from mutations in
multiple domains. Many of the mutations are located far from the dNTP binding
sites. These changes inhibit drug function by altering the conformation of the
target protein in a manner analogous to those conformational changes that may be
induced by an allosteric inhibitor.

232/116
Table 5 summarizes the mutations that alter the function of non-nucleoside
inhibitor drugs
Table 5
Location and postulated mechanism of amino acid substitutions which confer
resistance to non-nucleoside analog inhibitors.

ala98gly 5b- 6 loop flexibility Pyridinone L-697661, Nevirapine
leul.00ile 5b- 6 loop -branch Pyridinone L-697661 Nevirapine, TIBO R82913
lyslolglu 5b- 6 loop charge Pyridinone. . . loop flexibility BHAP U-87201
lys238thr 14 charge BHAP U-87201
trp266X -thumb TIBO R82913
232/116
It is evident from these examples that the substitutions which inhibit drug functions
are distributed across several domains. Different inhibitory mechanisms have been
postulated in domains throughout the protein, based on the three-dimensional
structure of the protein. Most involve conforniational disruption of. .

Thyrotropin receptor Naturally occurring antibodies against the thyrotropin
receptor can cause activation of thyroid function (Grave's disease) or inhibition of
thyroid function (Hashimoto's disease). The sites within the thyrotropin receptor
that are targeted by these natural antibodies have been mapped in detail and have
been tested with monoclonal antibodies. Most of the inhibitory antibodies do not
interfere with binding of thyrotropin to its receptor, and thus, are allosteric rather
than competitive inhibitors. Several independent classes of inhibitory antibodies
have been identified that bind to epitopes within different domains of the receptor.

can be deleted by site-directed mutagenesis without disrupting the function of the receptor. These experiments provide an explicit precedent for achieving allosteric inhibitory effects from ligands that target widely dispersed sequences within the protein.

Thermus aquaticus DNA polymerase The inhibitory activity of 24 monoclonal antibodies to Thermus aquaticus DNA polymerase has been investigated. The antibodies recognized 13 non-overlapping epitopes. Antibody binding to eight epitopes was inhibitory. Inhibitory antibodies mapped to several distinct domains, including the 5'nuclease domain, the polymerase domain and the boundary region between the 5'nuclease and polyinerase domains. Some antibodies recognized epitopes overlapping the DNA binding groove of the polymerase. Significantly, the inhibitory antibodies recognized epitopes constituting as much as 50% of the Taq polymerase surface, and the non-inhibitory antibodies a further -25%.

. . .

the pharmaceutical industry has worked to develop chemically modified penicillins and cephalosporins to elude inactivation by P-lactamases. In addition, a P-lactarnase inhibitor (clavulanic acid) has also been introduced into clinical use.

. . .

associated with drug resistance distributed evenly across the 740 amino acids of the protein. The mechanism by which some of these substitutions inhibit katG function can be inferred from the structure of the homologous yeast and E. coli enzymes and knowledge of the catalytic. . .

The application of small molecule inhibitor identification is specifically discussed in Example 39 below in connection with the methylguanine methyltransferase gene.

C. Antibody Inhibition.

Antibody inhibitors are most effective when they are directed against cell surface proteins or receptors. If the essential protein produced by the targeted allele is not a cell surface protein or receptor, the development of antibody inhibitors may also require the use of a special antibody-delivery system to facilitate entry of the antibody into the tumor cells. The plasma. . . the structure of the variable region of allele specific antibodies can be used as the basis for design of smaller allele specific inhibitory molecules.

. . .

receptors or other polypeptides essential for cell viability. Methods for screening peptide sequences

which have high specificity for binding to, and functional inhibition of, a specific polypeptide target have been well described previously. Scott, J.K. and Smith G.P., Searching for Peptide Ligands with an Epitope. . . by phage display of polypeptide sequences as well as direct screening of peptides or mixtures of synthetic peptides for binding to or inhibition of the target Rinctional polypeptide.

.

Ribozymes

Oligonucleotides or oligonucleotide analogs which interact with complementary sequences of cellular target DNA or RNA can be synthesized and used to inhibit or control gene expression at the levels of transcription or translation. The oligonucleotides of this invention can be either oligodeoxyribonucleotides or oligoribonucleotides, or. . . they can act enzymatically, such as ribozymes. Both antisense RNA and DNA can be used in this capacity as chemotherapeutic agents for inhibiting gene transcription or translation. Trojan, J., et aL, Treatment and prevention of rat glioblastoma, by immunogenic C6 cells expressing antisense insulin-like growth. . .

Inhibitory complementary oligonucleotides may be used as inhibitors for cancer therapeutics because of their high specificity and lack of toxicity.

Included in the scope of the invention are oligoribonucleotides, including antisense RNA and DNA molecules and ribozymes that function to inhibit expression of an essential gene in an allele specific manner. Anti-sense RNA and DNA molecules act to directly block the translation of. . .

A specific application of generating inhibitors which are either complementary oligonucleotides or inhibitory oligopeptides is described in Holzmayer, Pestov, and Roninson, Isolation of dominant negative mutants and inhibitory antisense RNA sequences by expression selection of random DNA fragments, Nucleic Acids Research 20:711-717 (1992). In this study, genetic suppressor elements (GSEs). . .

Preferred oligonucleotide inhibitors include oligonucleotide analogues which are resistant to degradation or hydrolysis by nucleases. These analogues include neutral, or nonionic, methylphosphonate analogues, which retain. . .

F, Gene Therapy

Nucleic acid molecules encoding oligonucleotide or polypeptide inhibitors will also be useftil in gene therapy (reviewed in Miller, Nature 357:455-460, (1992). Miller indicates that advances have resulted in practical approaches. . .

A nucleic acid sequence encoding an inhibitor may be administered utilizing an ex vivo approach

whereby cells are removed from an animal, transduced with the nucleic acid
sequence and reimplanted. . .

Many nonviral techniques for the delivery of a nucleic acid sequence encoding an
inhibitor into a cell can be used, including direct naked DNA uptake (e.g., Wolff et
al., Science 247: 1465-1468, 1990), receptor-mediated DNA. . .
. . .
its simplest form, gene transfer can be performed by simply injecting minute
amounts of DNA (e.g., a plasmid vector encoding an inhibitor) into the nucleus of a
cell, through a process of microinjection. Capecchi MR, Cell 22:479-88 (1980).

232/116
In another preferred embodiment, a vector having nucleic acid sequences encoding
an allele specific inhibitor is provided in which the nucleic acid sequence is
expressed only in specific tissue. Examples or methods of achieving tissue-specific
gene expression. . .

V11. Utility of allele-specific inhibitors of essential genes
A, Conditions susceptible to therapy.

The fraction of all cancers could be treated with allele specific inhibitors directed
against allele specific essential gene targets is a function of the frequency of the
target allele and the frequency of LOH.. . . exist in two allelic forms, each with an allele
frequency of 0.5 so that half the population would be heterozygous. An inhibitor of
one allele of such an ideal target would be a useful agent for 25% of all cancer
patients. An inhibitor of the other allele of the same ideal target would be
therapeutic for an additional 25% of all patients, making 50%. . .

Allele specific inhibitors of both alleles of such targets would be expected to
address 0.4 x 0.5 = 0.2 or 20% of the relevant. . .
<------User Break------>

```
=> s actin
         15854 ACTIN
           208 ACTINS
L24      15915 ACTIN
                (ACTIN OR ACTINS)

=> s stabil?
L25     282338 STABIL?

=> s ewing?
L26       3185 EWING?

=> s l26 and l24
L27       1098 L26 AND L24

=> s l27 and l25
L28       1004 L27 AND L25
```

```
=> s l24/ab
           151 ACTIN/AB
             1 ACTINS/AB
L29        152 (ACTIN/AB)
                ((ACTIN OR ACTINS)/AB)

=> s l29 and l26
L30          5 L29 AND L26

=> s l30 and l25
L31          5 L30 AND L25

=> d ibib 1-5

L31    ANSWER 1 OF 5     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2006029046 PCTFULL  ED 20060403  EW 200611
TITLE (ENGLISH):         USE OF LEPTIN IN WOUND HEALING
TITLE (FRENCH):          UTILISATION DE LEPTINE DANS LA GUERISON DE PLAIE
INVENTOR(S):             SIERRA-HONIGMANN, Maria Rocio, 656 Camino de la Luna,
                         Thousand Oaks, California 91320, US
PATENT ASSIGNEE(S):      YALE UNIVERSITY, Office of Cooperative Research, 433
                         Temple Street, New Haven, Connecticut 06511, US
AGENT:                   LEVY, Seth, D. et al.$, Suite 2400, 865 South Figueroa
                         Street, Los Angeles, California 90017-2566;
                         90017-2566$, US
LANGUAGE OF FILING:      English
LANGUAGE OF PUBL.:       English
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 2006029046         A2 20060316
DESIGNATED STATES
       W:                AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO
                         CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR
                         HU ID IL IN IS JP KE KG KM KP KR KZ LC LK LR LS LT LU
                         LV MA MD MG MK MN MW MX MZ NA NG NI NO NZ OM PG PH PL
                         PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA
                         UG US UZ VC VN YU ZA ZM ZW
       RW (ARIPO):       BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW
       RW (EAPO):        AM AZ BY KG KZ MD RU TJ TM
       RW (EPO):         AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT
                         LT LU LV MC NL PL PT RO SE SI SK TR
       RW (OAPI):        BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.:       WO 2005-US31455       A  20050902
PRIORITY INFO.:          US 2004-60607115         20040903

L31    ANSWER 2 OF 5     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2005042726 PCTFULL  ED 20050519  EW 200519
TITLE (ENGLISH):         METHODS FOR MODULATING AN IMMUNE RESPONSE BY MODULATING
                         KRC ACTIVITY
TITLE (FRENCH):          METHODES PERMETTANT DE MODULER UNE REPONSE IMMUNITAIRE
                         PAR MODULATION DE L'ACTIVITE DE KRC
INVENTOR(S):             GLIMCHER, Laurie, H., 51 Hampshire Street, West Newton,
                         MA 02165, US [US, US];
                         OUKKA, Mohamed, 46 Englewood Avenue, Brighton, MA
                         02146, US [US, US]
PATENT ASSIGNEE(S):      PRESIDENT AND FELLOWS OF HARVARD COLLEGE, 1350
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                         US [US, US], for all designates States except US;
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                         MA 02165, US [US, US], for US only;
                         OUKKA, Mohamed, 46 Englewood Avenue, Brighton, MA
                         02146, US [US, US], for US only
```

AGENT: DECONTI, Giulio, A.$, Lahive & Cockfield, LLP, 28 State Street, Boston, MA 02109$, US

LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2005042726	A2	20050512

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
RW (ARIPO): BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LU MC NL PL PT RO SE SI SK TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2004-US36641 A 20041103
PRIORITY INFO.: US 2003-10/701,401 20031103

L31 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2003027235 PCTFULL ED 20030410 EW 200314
TITLE (ENGLISH): AFAP SEQUENCES, POLYPEPTIDES, ANTIBODIES AND METHODS
TITLE (FRENCH): SEQUENCES AFAP, POLYPEPTIDES, ANTICORPS ET PROCEDES ASSOCIES
INVENTOR(S): FLYNN, Daniel, C., 418 Shawnee Drive, Morgantown, WV 26508-0911, US
PATENT ASSIGNEE(S): WEST VIRGINIA UNIVERSITY RESEARCH CORPORATION, P.O. Box 6216, 201 Chestnut Ridge Research Building, Morgantown, WV 26506-6216, US [US, US]
AGENT: SPAR, Elizabeth, N.$, Palmer & Dodge LLP, 111 Huntington Avenue, Boston, MA 02199-7613$, US

LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2003027235	A2	20030403

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM
RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-US29559 A 20020918
PRIORITY INFO.: US 2001-60/323,866 20010921

L31 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2002102846 PCTFULL ED 20030115 EW 200252
TITLE (ENGLISH): PHARMACEUTICAL COMPOSITION FOR DIAGNOSIS, PREVENTION OR TREATMENT OF A TUMOROUS STATE, COMPRISING A MODULATOR OF THE ACTIN POLYMERISATION STATE
TITLE (FRENCH): COMPOSITION PHARMACEUTIQUE POUR LE DIAGNOSTIC, LA PREVENTION OU LE TRAITEMENT D'UNE PATHOLOGIE TUMORALE, COMPRENANT UN AGENT MODULATEUR DE L'ETAT DE

POLYMERISATION DE L'ACTINE

INVENTOR(S): AUCLAIR, Christian, 22, avenue Parmentier, F-75011 Paris, FR [FR, FR];
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CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE -CNRS-, 3, rue Michel Ange, F-75794 Paris Cedex 16, FR [FR, FR], for all designates States except US;
AUCLAIR, Christian, 22, avenue Parmentier, F-75011 Paris, FR [FR, FR], for US only;
AMSELLEM, Valerie, 103, avenue Philippe-Auguste, F-75011 Paris, FR [FR, FR], for US only;
HERVY, Martial, 5, rue de l'Amiral Mouchez, F-75013 Paris, FR [FR, FR], for US only;
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AGENT: BRESSE, Pierre$, Bresse-Majerowicz, 3, avenue de l'Opera, F-75001 Paris$, FR

LANGUAGE OF FILING: French
LANGUAGE OF PUBL.: French
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2002102846	A2	20021227

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-FR2106 A 20020618
PRIORITY INFO.: FR 2001-01/07976 20010618

L31 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999022028 PCTFULL ED 20020515
TITLE (ENGLISH): MODULATORS OF ACTIN
TITLE (FRENCH): MODULATEURS D'ACTINE
INVENTOR(S): KING, Mary-Claire;
LYNCH, Eric, D.;
LEE, Ming, K.;
MORROW, Jan, E.;
WELCSH, Piri, L.;
LEON, Pedro, E.
PATENT ASSIGNEE(S): THE UNIVERSITY OF WASHINGTON;
THE UNIVERSITY OF COSTA RICA
LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9922028	A1	19990506

DESIGNATED STATES
W: CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-US23024 . A 19981029
PRIORITY INFO.: US 1997-60/063,737 19971029
US 1998-09/080,897 19980518

=> d kwic 31
5 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
The answer numbers requested are not in the answer set.
ENTER ANSWER NUMBER OR RANGE (1):eng
ANSWER NUMBERS NOT CORRECTLY SPECIFIED
Enter an answer number, Example: 10
several answer numbers, Example: 3,7,10
a range of answer numbers, Example: 5-10
or a combination of these. Example: 3,7,9-10,15
ENTER ANSWER NUMBER OR RANGE (1):end

=> d kwic 3

L31 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ABEN The present invention comprises reagents and methods which target actin filaments or the cellular signals that control actin filament integrity. Specifically, the invention provides novel actin binding polypeptides (e.g., human AFAP polypeptides), antibodies which specifically recognize the same, nucleic acids encoding the same, and methods for. . .

DETD . . . aspect, the pathology is cancer, e.g., such as breast cancer, colon cancer,
prostate cancer, lung cancer, a cancer involving neural cells, Ewing sarcoma and
rhabdomyosarcoma.
. . .
acids comprising one or more of modified bases, sugars, and intermicleotide linkages
which preferably have the substantially the same or enhanced stability and/or specificity for a
target nucleic acid as the nucleic acids from which they are derived.
. . .
Antisense nucleic acids can also be
chemically synthesized and can be deoxynucleotides or modified forms thereof which are
selected to have enhanced stability in vivo.
. . .
activated in a number of human cancers including breast cancer, colon cancer, prostate cancer, lung cancer (e.g., small lung cell carcinoma), neuroblastoma,
Ewing sarcoma and rhabdomyosarcoma (Cartwright et al., 1990, supra; Rosen et al., 1986,
supra).
. . .
breast cancer, colon cancer, prostate cancer, lung cancer
(e.g., small lung cell carcinoma), a cancer involving neural cells (e.g., such as neuroblastoma),
Ewing sarcoma and rhabdomyosarcoma.
. . .
forms thereof. In one aspect, the condition is cancer (e.g., such as breast cancer, colon cancer, prostate cancer, lung cancer,

neuroblastoma, Ewing sarcoma
and rhabdomyosarcoma). In another aspect, the condition is a
neurological disease (which can
47
The agents, agonists, and antagonists may be formulated. . .
. . .
and coverslips and observed under confocal microscopy (Zeiss,
Oberkochen, Germany). Samples for negative staining were adsorbed to
grids coated with
nitrocellulose and stabilized with carbon (Ernest F. Fullam,
Latham, NY). Unbound protein was
removed by successive washes with buffer and water before staining with.
. .

CLMEN. . . said cancer is selected from the group
consisting of. breast cancer, colon cancer, prostate cancer, lung
cancer, a cancer
involving neural cells, Ewing sarcoma and rhabdomyosarcoma.

=> d kwic 5

L31 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ABEN The invention provides methods and compositions which find use, i(inter
alia), for modulating
the stabilization of actin filaments. The
compositions may comprise one or more polypeptide moieties
derived from a novel human diaphanous polypeptide and/or one or. . .
ABFR L'invention concerne des procedes et des compositions permettant, entre
autres choses, de
moduler la stabilisation des filaments d'actine. Ces
compositions peuvent comprendre une ou
plusieurs fractions de polypeptide derivees d'un nouveau polypeptide
diaphane de l'homme. . .

DETD INTRODUCTION
Field of the Invention
The invention relates to a class of polypeptides involved in actin
stabilization.
. . .
of the Invention
The actin cytoskeleton plays a central role in defining cellular
structure and effecting
dynamic changes in morphology. By selectively stabilizing and
destabilizing actin
polymerization, the cell is able to effect a wide range of structural
reorganization and effect
phenomena such as cell. . .

the progress of many pathogenic infections, invasion and metastisis of
neoplasia, fertilization,
clotting and wound repair, etc., the stability of actin
polymerization is a choice target for
therapuetic intervention. In fact, potent drugs effecting actin filament
destabilization and
stabilization such as fungal-derived alkaloids including the
cytochalasins and phalloidins are
well known. Here we disclose a new family of modulators of actin polymer
stabilization
derived from a novel human diaphanous protein and gene.

SUMMARY OF THE INVENTION
The invention provides methods and compositions which find use. inter
alia, for
modulating the stabilization of actin filaments. The

compositions may comprise one or more
polypeptide moieties derived from a novel human diaphanous polypeptide
and/or one. . .
. . .
other polypeptide moieties, complexed in a wide variety of
covalent and/or non-covalent associations and binding complexes, etc.,
which may provide
enhanced activity, stability, availability, targeting, etc.
. . .
polypeptide
hDial-del-15: CYCLIN B2 - residues 1141-1171 of SEQ ID NO:2 fusion
polypeptide
The invention provides methods and compositions of selectively
modulating
cytoskeletal de/stabilization and/or the effective
concentration of a human diaphanous protein
within a target cell. The general methods involve introducing into the
target. . . the human diaphanous polypeptide moiety, the modulator
may
comprise a wide variety of additional moieties, including moieties which
provide for
detection, targeting, stability, proteolytic resistance, etc.
Preferred modulators demonstrate
cytoskelatal de/stabilization with several alternative methods
of introduction, including direct
medium uptake, uptake facilitated by chaotropic agents including
detergents (e.g. TWEEN20,
etc.), guanadine salts,. . ..
. . .
to a probe specific for the binding agent. Agents of
particular interest modulate human diaphanous polypeptide function, e.g.
human diaphanous
5
polypeptide-dependent actin de/stabilization.
. . .
usually RNA or DNA, it is often advantageous to use nucleic acids
comprising other bases or nucleotide analogs to provide modified
stability, etc.
. . .
3.0 were transferred to a UNIX-based Sun workstation for cont-ig'
assembly and blast analysis. The computer program PHRED (Green P and
Ewing B. 1996.
. . .
phrap.docs/ phred.html) was used to assign bases
to the electropherograms. After eliminating vector sequences, the
program PHRAP (Green P
1 0 and Ewing B. 1996. http:H www.bozeman.mbt.washington.edu/
phrap.docs/ phrap.html) was
used to analyze the sequences, identify overlapping individual
sequences, and assemble them
into contigs. To. . .
. . .
daily blood and peritoneal sample to evaluate peritoneal fluid cell
counts,
hernatological cell counts, serum chemistries, bacterial cultures as
needed, vector stability,
viral uptake by cells, expression of hDial gene and presence of
antibodies to vector envelope
proteins. At four week intervals patients are. . .

Detection of vector stability and expression. DNA is prepared
from cell samples by
hypotonic lysis, digestion with proteinase K (Boehringer Mannheim,
Indianapolis. Indiana)
and SDS, followed. . .

PCR primers specific for the neo sequences within the LXSN-hDialsv vector are
employed for determination of vector presence and stability within patient samples. RT-PCR
is performed by our published methods (Thompson, M. E., et al. Nature Genetics 9, 444-
450] 1995.).

```
=> s ewing sarcoma or (ewing? sarcoma
UNMATCHED LEFT PARENTHESIS 'OR (EWING?'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s ewing sarcoma or (ewing? sarcoma)
          3035 EWING
           132 EWINGS
          3112 EWING
                 (EWING OR EWINGS)
         18118 SARCOMA
          5088 SARCOMAS
             5 SARCOMATA
         19804 SARCOMA
                 (SARCOMA OR SARCOMAS OR SARCOMATA)
           392 EWING SARCOMA
                 (EWING(W)SARCOMA)
          3185 EWING?
         18118 SARCOMA
          5088 SARCOMAS
             5 SARCOMATA
         19804 SARCOMA
                 (SARCOMA OR SARCOMAS OR SARCOMATA)
           400 EWING? SARCOMA
                 (EWING?(W)SARCOMA)
L32        400 EWING SARCOMA OR (EWING? SARCOMA)

=> d his

     (FILE 'HOME' ENTERED AT 14:41:45 ON 17 APR 2006)

     FILE 'REGISTRY' ENTERED AT 14:41:55 ON 17 APR 2006
                E "DOLASTATIN"/CN 25
L1            1 S E6

     FILE 'CAPLUS' ENTERED AT 14:42:50 ON 17 APR 2006
L2        52669 S ACTIN
L3          812 S COFILIN
L4      1968300 S ANTAG? OR INHIBIT?
L5          222 S L4 (L) L3
L6         1659 S EWING?
L7            1 S L6 AND L5
L8           22 S L1
L9            0 S L8 AND L6
L10         224 S ZYXIN
L11           3 S L10 AND L6
L12           6 S L3 AND L6
L13           4 S L12 AND L4
L14         989 S PHOSPHOINOSITOL?
L15           0 S L14 AND L6
L16          98 S PHOSPHOTIDYLINOSITOL
L17           0 S L15 AND L6

     FILE 'PCTFULL' ENTERED AT 14:49:15 ON 17 APR 2006
L18         188 S COFILIN
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L19         3185 S EWING?
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L22           19 S L20 AND L21
L23            4 S L22 NOT PY>2001
L24        15915 S ACTIN
L25       282338 S STABIL?
L26         3185 S EWING?
L27         1098 S L26 AND L24
L28         1004 S L27 AND L25
L29          152 S L24/AB
L30            5 S L29 AND L26
L31            5 S L30 AND L25
L32          400 S EWING SARCOMA OR (EWING? SARCOMA)

=> s l32 and l24
L33          165 L32 AND L24

=> s l33 and l25
L34          137 L33 AND L25

=> s l34 not py>2001
        488865 PY>2001
L35           54 L34 NOT PY>2001

=> s l35 and l29
L36            0 L35 AND L29

=> s l24/clm
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=> s l37 and l35
L38            5 L37 AND L35

=> s l24/ti
L39           44 (ACTIN/TI)

=> s l39 and l35
L40            0 L39 AND L35

=> d ibib l38 1-5

L38    ANSWER 1 OF 5     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2001055368 PCTFULL  ED 20020827
TITLE (ENGLISH):         NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH):          ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S):             ROSEN, Craig, A.;
                         BARASH, Steven, C.;
                         RUBEN, Steven, M.
PATENT ASSIGNEE(S):      HUMAN GENOME SCIENCES, INC.;
                         ROSEN, Craig, A.;
                         BARASH, Steven, C.;
                         RUBEN, Steven, M.
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
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                         WO 2001055368         A1 20010802
DESIGNATED STATES
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US 2000-60/254,097 20001211
US 2001-60/259,678 20010105

L38 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001055328 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055328	A2	20010802

DESIGNATED STATES
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APPLICATION INFO.: WO 2001-US1359 A 20010117
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US 2000-60/254,097	20001211
US 2001-60/259,678	20010105

L38 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001055201 PCTFULL ED 20020827
TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES
TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS
INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001055201	A1	20010802

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US 2000-60/246,478	20001108
US 2000-60/246,524	20001108
US 2000-60/246,523	20001108
US 2000-60/249,299	20001117
US 2000-60/249,210	20001117
US 2000-60/249,216	20001117
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US 2000-60/249,264	20001117
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US 2000-60/249,300	20001117
US 2000-60/249,265	20001117
US 2000-60/250,391	20001201
US 2000-60/250,160	20001201
US 2000-60/256,719	20001205

	US 2000-60/251,030 20001205
	US 2000-60/251,988 20001205
	US 2000-60/251,479 20001206
	US 2000-60/251,869 20001208
	US 2000-60/251,856 20001208
	US 2000-60/251,868 20001208
	US 2000-60/251,990 20001208
	US 2000-60/251,989 20001208
	US 2000-60/254,097 20001211
	US 2001-60/259,678 20010105

L38 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 2001054733 PCTFULL ED 20020827

TITLE (ENGLISH): NUCLEIC ACIDS, PROTEINS AND ANTIBODIES

TITLE (FRENCH): ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS

INVENTOR(S): ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.

PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;
ROSEN, Craig, A.;
BARASH, Steven, C.;
RUBEN, Steven, M.

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001054733	A1	20010802

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:	WO 2001-US1312	A	20010117
PRIORITY INFO.:	US 2000-60/179,065		20000131
	US 2000-60/180,628		20000204
	US 2000-60/184,664		20000224
	US 2000-60/186,350		20000302
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	US 2000-60/190,076		20000317
	US 2000-60/198,123		20000418
	US 2000-60/205,515		20000519
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US 2000-60/249,264	20001117
US 2000-60/249,209	20001117
US 2000-60/249,300	20001117
US 2000-60/249,265	20001117
US 2000-60/250,391	20001201
US 2000-60/250,160	20001201
US 2000-60/256,719	20001205
US 2000-60/251,030	20001205
US 2000-60/251,988	20001205
US 2000-60/251,479	20001206
US 2000-60/251,869	20001208
US 2000-60/251,856	20001208
US 2000-60/251,868	20001208
US 2000-60/251,990	20001208
US 2000-60/251,989	20001208
US 2000-60/254,097	20001211
US 2001-60/259,678	20010105

L38 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001053514 PCTFULL ED 20020827
TITLE (ENGLISH): TOXICANT-INDUCED DIFFERENTIAL GENE EXPRESSION
TITLE (FRENCH): EXPRESSION GENETIQUE DIFFERENTIELLE INDUITE PAR SUBSTANCES TOXIQUES
INVENTOR(S): REIDHAAR-OLSON, John, F.
PATENT ASSIGNEE(S): GLAXO GROUP LIMITED;
REIDHAAR-OLSON, John, F.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001053514	A1	20010726

DESIGNATED STATES
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA

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                         GN GW ML MR NE SN TD TG
APPLICATION INFO.:       WO 2001-US1920       A  20010119
PRIORITY INFO.:          US 2000-09/489,220       20000121


=>

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=> LOG Y


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LOGINID:SSSPTA1642BJF

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  DEC 23   New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
                   USPAT2
 NEWS  4  JAN 13   IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
 NEWS  5  JAN 13   New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
                   INPADOC
 NEWS  6  JAN 17   Pre-1988 INPI data added to MARPAT
 NEWS  7  JAN 17   IPC 8 in the WPI family of databases including WPIFV
 NEWS  8  JAN 30   Saved answer limit increased
 NEWS  9  FEB 21   STN AnaVist, Version 1.1, lets you share your STN AnaVist
                   visualization results
 NEWS 10  FEB 22   The IPC thesaurus added to additional patent databases on STN
 NEWS 11  FEB 22   Updates in EPFULL; IPC 8 enhancements added
 NEWS 12  FEB 27   New STN AnaVist pricing effective March 1, 2006
 NEWS 13  FEB 28   MEDLINE/LMEDLINE reload improves functionality
 NEWS 14  FEB 28   TOXCENTER reloaded with enhancements
 NEWS 15  FEB 28   REGISTRY/ZREGISTRY enhanced with more experimental spectral
                   property data
 NEWS 16  MAR 01   INSPEC reloaded and enhanced
 NEWS 17  MAR 03   Updates in PATDPA; addition of IPC 8 data without attributes
 NEWS 18  MAR 08   X.25 communication option no longer available after June 2006
 NEWS 19  MAR 22   EMBASE is now updated on a daily basis
 NEWS 20  APR 03   New IPC 8 fields and IPC thesaurus added to PATDPAFULL
 NEWS 21  APR 03   Bibliographic data updates resume; new IPC 8 fields and IPC
                   thesaurus added in PCTFULL
 NEWS 22  APR 04   STN AnaVist $500 visualization usage credit offered
 NEWS 23  APR 12   LINSPEC, learning database for INSPEC, reloaded and enhanced
 NEWS 24  APR 12   Improved structure highlighting in FQHIT and QHIT display
                   in MARPAT
 NEWS 25  APR 12   Derwent World Patents Index to be reloaded and enhanced during
                   second quarter; strategies may be affected
```

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 NEWS EXPRESS  FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
               V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
               http://download.cas.org/express/v8.0-Discover/

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 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

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FILE 'HOME' ENTERED AT 16:12:12 ON 17 APR 2006

=> file pctfull
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'PCTFULL' ENTERED AT 16:12:30 ON 17 APR 2006
COPYRIGHT (C) 2006 Univentio

FILE LAST UPDATED:          11 APR 2006      <20060411/UP>
MOST RECENT UPDATE WEEK:        200614        <200614/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
    SEE
    http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE
    (last updated April 10, 2006) <<<

=> s jasplakinolide
           171 JASPLAKINOLIDE
             1 JASPLAKINOLIDES
L1         171 JASPLAKINOLIDE
               (JASPLAKINOLIDE OR JASPLAKINOLIDES)

=> s ewing? (2W) sarcoma
          3185 EWING?
         18118 SARCOMA
          5088 SARCOMAS
             5 SARCOMATA
         19804 SARCOMA
               (SARCOMA OR SARCOMAS OR SARCOMATA)
L2        1574 EWING? (2W) SARCOMA

=> s l2 and l1
L3          36 L2 AND L1

=> s l3 not py>2001
        488865 PY>2001
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L4            1 L3 NOT PY>2001

=> d ibib

L4     ANSWER 1 OF 1      PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2000071135 PCTFULL  ED 20020515
TITLE (ENGLISH):         ANTI-TUMOR COMPRISING BOROPROLINE COMPOUNDS
TITLE (FRENCH):          AGENTS ANTI-TUMORALES CONTENANT DES COMPOSES DE
                         BOROPROLINE
INVENTOR(S):             WALLNER, Barbara, P.;
                         MILLER, Glenn
PATENT ASSIGNEE(S):      POINT THERAPEUTICS, INC.
LANGUAGE OF PUBL.:       English
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 2000071135         A1 20001130
DESIGNATED STATES
       W:                AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ
                         DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
                         JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
                         MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
                         TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ
                         TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK
                         ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM
                         GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:       WO 2000-US14505       A  20000525
PRIORITY INFO.:          US 1999-60/135,861       19990525


=> d kwic

L4     ANSWER 1 OF 1      PCTFULL   COPYRIGHT 2006 Univentio on STN

DETD  . . . myxoid liposarcomas and pleiomorphic
       liposarcomas), leiomyosarcomas, rhabdomyosarcomas, malignant peripheral
       nerve sheath
       tumors (also called malignant schwannomas, neurofibrosarcomas, or
       neurogenic sarcomas),
       Ewing's tumors (including Ewing's sarcoma of bone,
       extraskeletal [not bone] Ewing's
       io sarcoma, and primitive neuroectoderinal tumor [PNET]),
       synovial sarcoma, angiosarconias,
       hemangiosarcomas, lymphangiosarcomas, Kaposi's sarcoma,
       hemangioendothelioma,
       fibrosarcoma, desmoid tumor (also called aggressive fibromatosis),
       dermatofibrosarcoma
       protuberans (DFSP),. . .
 . . .
       immunostimulant peptides-, insulin-like growth factor-I receptor
       inhibitoi, interferon
       agonists; interferons; interleukins; iobenguane; lododoxorubicin;
       lporneanol, 4-; irinotecan;
       iroplact; irsogladine; isobengazole; isohomohalicondrin B; itasetron;
       jasplakinolide;
       kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin;
       lenograstim; lentinan sulfate;
       leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha
       interferon; leuprolide +
       estrogen + progesterone; leuprorelin;. . .


=> s hepatocarcinoma? or mesenchymal or neuroectodermal
          463 HEPATOCARCINOMA?
```

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          4765 MESENCHYMAL
             1 MESENCHYMALS
          4765 MESENCHYMAL
                 (MESENCHYMAL OR MESENCHYMALS)
           922 NEUROECTODERMAL
             1 NEUROECTODERMALS
           922 NEUROECTODERMAL
                 (NEUROECTODERMAL OR NEUROECTODERMALS)
L5        5608 HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL

=> s l5 and l4
L6           1 L5 AND L4

=> d kwic\
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The following are valid formats:

ALL, MAX--------BIB plus IND plus ABS plus TX
ALLG------------ALL, MAX plus GI
BIB-------------AN, ED, UP, EW, UW, TIEN, TIFR, TIDE, TIES, IN, PA, LA, LAF
                DT, PI, DS, AI, PRAI
BIBG------------BIB plus GI
IND, IPC--------ICM, ICS
ABS-------------ABEN, ABF, ABFR, ABDE, ABES
TX--------------DETD, CLM
IALL,IMAX-------ALL indented with text labels
IALLG,IMAXG-----IALL, IMAX plus GI
DALL------------Delimited ALL format
STD-------------BIB plus IND
STDG------------STD plus GI
ISTD------------STD indented with text labels
ISTDG-----------ISTD plus GI
BRIEF-----------BIB plus ABS
BRIEFG----------BIB plus ABS plus GI
IBRIEF----------BRIEF indented with text labels
IBRIEFG---------IBRIEF plus GI
SCAN------------TI (random display without AN)
TRIAL (TRI)-----FA, TI, CLMN, DETN
SAMPLE (SAM)----FA, TI, CLMN, DETN
FREE------------FA, TI, CLMN, DETN
ENTER DISPLAY FORMAT (STD):kwic

L6     ANSWER 1 OF 1     PCTFULL   COPYRIGHT 2006 Univentio on STN

DETD  . . . epithelium eductus semicircularis, enamel epithelium, false
       epithelium,
       germinal epithelium, gingival epithelium, glandular epithelium,
       glomerular epithelium,
       laminated epithelium, epithelium of lens, epithelium lentis,
       mesenchymal epithelium,
       olfactory epithelium, pavement epithelium, pigmentary epithelium,
       pigmented epithelium,
       protective epithelium, pseudostratified epithelium, pyramidal
       epithelium, respiratory
       epithelium, rod epithelium, serniniferous epithelium, sense epithelium,.
       . .
 . . .
       gelatinous carcinoma, giant cell
       carcinoma, gigantocellulare, glandular carcinoma, granulosa. cell
       carcinoma, hair-matrix
       carcinoma, hematoid carcinoma, hepatocellular carcinoma (also called
       hepatoma, malignant
       hepatoma and hepatocarcinoma), Mirthle cell carcinoma, hyaline
       carcinoma, hypernephroid
```

carcinoma, infantile embryonal carcinoma, carcinoma in situ, intraepidermal carcinoma,
intraepithelial carcinoma, Krompecher's carcinoma, Kulchitzky-cell carcinoma, lenticular
carcinoma,. . .
. . .
characterized by an abnormal mammalian cell proliferation to be treated by the methods of the invention include sarcomas. Sarcomas are rare mesenchymal
neoplasms that arise in bone and soft tissues. Different types of sarcomas are recognized and
these include: liposarcomas (including myxoid liposarcomas and pleiomorphic
liposarcomas), leiomyosarcomas, rhabdomyosarcomas, malignant peripheral nerve sheath
tumors (also called malignant schwannomas, neurofibrosarcomas, or neurogenic sarcomas),
Ewing's tumors (including Ewing's sarcoma of bone, extraskeletal [not bone] Ewing's
io sarcoma, and primitive neuroectoderinal tumor [PNET]), synovial sarcoma, angiosarconias,
hemangiosarcomas, lymphangiosarcomas, Kaposi's sarcoma, hemangioendothelioma,
fibrosarcoma, desmoid tumor (also called aggressive fibromatosis), dermatofibrosarcoma
protuberans (DFSP),. . .
. . .
immunostimulant peptides-, insulin-like growth factor-I receptor inhibitoi, interferon
agonists; interferons; interleukins; iobenguane; lododoxorubicin; 1porneanol, 4-; irinotecan;
iroplact; irsogladine; isobengazole; isohomohalicondrin B; itasetron; jasplakinolide;
kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin; lenograstim; lentinan sulfate;
leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha interferon; leuprolide +
estrogen + progesterone; leuprorelin;. . .

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=> d his

     (FILE 'HOME' ENTERED AT 16:12:12 ON 17 APR 2006)

     FILE 'PCTFULL' ENTERED AT 16:12:30 ON 17 APR 2006
L1          171 S JASPLAKINOLIDE
L2         1574 S EWING? (2W) SARCOMA
L3           36 S L2 AND L1
L4            1 S L3 NOT PY>2001
L5         5608 S HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL
L6            1 S L5 AND L4

=> s l5 and l1
L7           37 L5 AND L1

=> s l7 not py>2001
        488865 PY>2001
L8            4 L7 NOT PY>2001

=> d ibib 1-4.

L8     ANSWER 1 OF 4      PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:         2001089520 PCTFULL  ED 20020826
TITLE (ENGLISH):          DEHYDROASCORBIC ACID FORMULATIONS AND USES THEREOF
TITLE (FRENCH):           FORMULATIONS D'ACIDE DEHYDROASCORBIQUE ET LEURS
```

UTILISATIONS
INVENTOR(S): OLSON, William, C.;
ISRAEL, Robert, J.;
BOYD, Thomas, A.
PATENT ASSIGNEE(S): PROGENICS PHARMACEUTICALS, INC.;
OLSON, William, C.;
ISRAEL, Robert, J.;
BOYD, Thomas, A.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001089520	A2	20011129

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2000-US41407 A 20001020
PRIORITY INFO.: US 2000-60/205,870 20000519

L8 ANSWER 2 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001029235 PCTFULL ED 20020820
TITLE (ENGLISH): TMS1 COMPOSITIONS AND METHODS OF USE
TITLE (FRENCH): COMPOSITIONS DU GENE TMS1 ET PROCEDES D'UTILISATION
INVENTOR(S): VERTINO, Paula, M.
PATENT ASSIGNEE(S): EMORY UNIVERSITY
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001029235	A2	20010426

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 2000-US28747 A 20001018
PRIORITY INFO.: US 1999-60/159,975 19991018

L8 ANSWER 3 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2000071135 PCTFULL ED 20020515
TITLE (ENGLISH): ANTI-TUMOR COMPRISING BOROPROLINE COMPOUNDS
TITLE (FRENCH): AGENTS ANTI-TUMORALES CONTENANT DES COMPOSES DE BOROPROLINE
INVENTOR(S): WALLNER, Barbara, P.;
MILLER, Glenn
PATENT ASSIGNEE(S): POINT THERAPEUTICS, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000071135	A1	20001130

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US14505 A 20000525
PRIORITY INFO.: US 1999-60/135,861 19990525

L8 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999004817 PCTFULL ED 20020515
TITLE (ENGLISH): CHEMOTHERAPY SYNERGISTIC AGENT
TITLE (FRENCH): AGENT SYNERGIQUE POUR CHIMIOTHERAPIE
INVENTOR(S): WINKELMAN, James, W.;
BRIDGES, Kenneth, R.
PATENT ASSIGNEE(S): BRIGHAM & WOMEN'S HOSPITAL, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9904817	A1	19990204

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-US15052 A 19980722
PRIORITY INFO.: US 1997-60/053,696 19970725
US 1997-60/054,148 19970725

=> d kwic 4

L8 ANSWER 4 OF 4 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . 91)
-
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcorna and osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basal. . . .
. . .
peptides; insulin-like
growth factor-I receptor inhibitor; interferon agonists; interferons; interleukins; iobenguane;
I 0 iododoxorubicin; ipomeanol, 4-; irinotecan; iroplact; irsogladine; isobengazole;
isohomohalicondrin B; itasetron; jasplakinolide; kahalalide F;
larnellarin-N triacetate;
lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin; letrozole; leukemia
inhibiting factor; leukocyte alpha interferon; leuprolide + estrogen + progesterone;
leuprorelin;. . .

CLMEN. . . and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas, including
leiornyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basocellular. . . .
. . .
and

lymphocytic lymphomas; neuroblastomas; oral cancer, including squarnous cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin
- 24 -
cancer, including melanoma, Kaposi's. . .
. . .
and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer'; rectal cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basocellular. . .

=> file caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	15.65	15.86

FILE 'CAPLUS' ENTERED AT 16:18:34 ON 17 APR 2006
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FILE COVERS 1907 - 17 Apr 2006 VOL 144 ISS 17
FILE LAST UPDATED: 16 Apr 2006 (20060416/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
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=> s jasplakinolide/cn
REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L10 118 L9

=> s jasplakinolide

```
          251 JASPLAKINOLIDE
            1 JASPLAKINOLIDES
L11         252 JASPLAKINOLIDE
                (JASPLAKINOLIDE OR JASPLAKINOLIDES)

=> s l11 or l10
L12         279 L11 OR L10

=> s hepatocarcinoma? or mesenchymal or neuroectodermal
          1409 HEPATOCARCINOMA?
         11238 MESENCHYMAL
          1281 NEUROECTODERMAL
L13      13848 HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL

=> s l13 and l12
L14           2 L13 AND L12

=> d ibib 1-2

L14  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:248055  CAPLUS
DOCUMENT NUMBER:          142:352644
TITLE:                    RhoA/ROCK Signaling Regulates Sox9 Expression and
                          Actin Organization during Chondrogenesis
AUTHOR(S):                Woods, Anita; Wang, Guoyan; Beier, Frank
CORPORATE SOURCE:         Canadian Institutes of Health Research Group in
                          Skeletal Development and Remodeling, Department of
                          Physiology and Pharmacology, University of Western
                          Ontario, London, ON, N6A 5C1, Can.
SOURCE:                   Journal of Biological Chemistry (2005), 280(12),
                          11626-11634
                          CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER:                American Society for Biochemistry and Molecular
                          Biology
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          73    THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2003:816528  CAPLUS
DOCUMENT NUMBER:          140:12638
TITLE:                    Two CD95 tumor classes with different sensitivities to
                          antitumor drugs
AUTHOR(S):                Algeciras-Schimnich, Alicia; Pietras, Eric M.;
                          Barnhart, Bryan C.; Legembre, Patrick; Vijayan,
                          Shrijay; Holbeck, Susan L.; Peter, Marcus E.
CORPORATE SOURCE:         The Ben May Institute for Cancer Research, University
                          of Chicago, Chicago, IL, 60637, USA
SOURCE:                   Proceedings of the National Academy of Sciences of the
                          United States of America (2003), 100(20), 11445-11450
                          CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:                National Academy of Sciences
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          26    THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> s ewing? (2W) sarcoma
          1659 EWING?
         36667 SARCOMA
          4162 SARCOMAS
           100 SARCOMATA
         38298 SARCOMA
```

```
                (SARCOMA OR SARCOMAS OR SARCOMATA)
L15       1277 EWING? (2W) SARCOMA

=> s l15 and l12
L16          0 L15 AND L12

=> s dolastatin 11/cn
   REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.



L18         22 L17

=> s dolastatin 11
            390 DOLASTATIN
             59 DOLASTATINS
            404 DOLASTATIN
                (DOLASTATIN OR DOLASTATINS)
         916607 11
L19         22 DOLASTATIN 11
                (DOLASTATIN(W)11)

=> s l19 or l18
L20         24 L19 OR L18

=> d his

     (FILE 'HOME' ENTERED AT 16:12:12 ON 17 APR 2006)

     FILE 'PCTFULL' ENTERED AT 16:12:30 ON 17 APR 2006
L1           171 S JASPLAKINOLIDE
L2          1574 S EWING? (2W) SARCOMA
L3            36 S L2 AND L1
L4             1 S L3 NOT PY>2001
L5          5608 S HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL
L6             1 S L5 AND L4
L7            37 S L5 AND L1
L8             4 S L7 NOT PY>2001

     FILE 'CAPLUS' ENTERED AT 16:18:34 ON 17 APR 2006
                S JASPLAKINOLIDE/CN

     FILE 'REGISTRY' ENTERED AT 16:18:43 ON 17 APR 2006
L9             1 S JASPLAKINOLIDE/CN

     FILE 'CAPLUS' ENTERED AT 16:18:43 ON 17 APR 2006
L10          118 S L9
L11          252 S JASPLAKINOLIDE
L12          279 S L11 OR L10
L13        13848 S HEPATOCARCINOMA? OR MESENCHYMAL OR NEUROECTODERMAL
L14            2 S L13 AND L12
L15         1277 S EWING? (2W) SARCOMA
L16            0 S L15 AND L12
                S DOLASTATIN 11/CN

     FILE 'REGISTRY' ENTERED AT 16:20:17 ON 17 APR 2006
L17            1 S DOLASTATIN 11/CN

     FILE 'CAPLUS' ENTERED AT 16:20:18 ON 17 APR 2006
L18           22 S L17
```

```
L19           22 S DOLASTATIN 11
L20           24 S L19 OR L18

=> s l20 and l13
L21           1 L20 AND L13

=> d ibib

L21  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2003:816528  CAPLUS
DOCUMENT NUMBER:          140:12638
TITLE:                    Two CD95 tumor classes with different sensitivities to
                          antitumor drugs
AUTHOR(S):                Algeciras-Schimnich, Alicia; Pietras, Eric M.;
                          Barnhart, Bryan C.; Legembre, Patrick; Vijayan,
                          Shrijay; Holbeck, Susan L.; Peter, Marcus E.
CORPORATE SOURCE:         The Ben May Institute for Cancer Research, University
                          of Chicago, Chicago, IL, 60637, USA
SOURCE:                   Proceedings of the National Academy of Sciences of the
                          United States of America (2003), 100(20), 11445-11450
                          CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:                National Academy of Sciences
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          26    THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d kwic

L21  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
AB    . . . half are type II. Most of the type I cell lines fall into a
      distinct class of tumor cells expressing mesenchymal-like genes,
      whereas the type II cell lines preferentially express epithelium-like
      markers. This suggests that type I and II tumor cells represent different
      stages of carcinogenesis that resemble the epithelial-mesenchymal
      transition. We then screened the National Cancer Institute database of
      >42,000 compds. for reagents with patterns of growth inhibition that.
      .
ST    soluble CD95ligand antitumor mesenchymal epithelial tumor actin
      tubulin disruption; antitumor resistance CD95 signaling gene expression
      carcinogenesis
IT    362-07-2, 2-Methoxyestradiol   1110-02-7, NSC 112167   2222-07-3,
      Cucurbitacin I   6040-19-3, Cucurbitacin A   6766-43-4, Cucurbitacin K
      33069-62-4D, Taxol, analog   82855-09-2D, Combretastatin, analog
      102396-24-7D, Jasplakinolide, analog   108675-64-5 111517-68-1,
      NSC 606195   141172-06-7   630400-59-8, NSC 666608   630400-60-1, NSC
      658831   630400-62-3, NSC 666606
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
         (two CD95 tumor classes with different sensitivities to antitumor
         drugs)


=>

---Logging off of STN---


=>
Executing the logoff script...


=> LOG Y
```

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	8.35	50.43
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.75	-0.75

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS	4	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	5	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	6	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	7	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS	8	JAN 30	Saved answer limit increased
NEWS	9	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS	10	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS	11	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS	12	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	13	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS	14	FEB 28	TOXCENTER reloaded with enhancements
NEWS	15	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	16	MAR 01	INSPEC reloaded and enhanced
NEWS	17	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS	18	MAR 08	X.25 communication option no longer available after June 2006
NEWS	19	MAR 22	EMBASE is now updated on a daily basis
NEWS	20	APR 03	New IPC 8 fields and IPC thesaurus added to PATDPAFULL
NEWS	21	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
NEWS	22	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS	23	APR 12	LINSPEC, learning database for INSPEC, reloaded and enhanced
NEWS	24	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS	25	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT

http://download.cas.org/express/v8.0-Discover/

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:03:09 ON 18 APR 2006

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'CAPLUS' ENTERED AT 09:03:17 ON 18 APR 2006
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FILE COVERS 1907 - 18 Apr 2006 VOL 144 ISS 17
FILE LAST UPDATED: 17 Apr 2006 (20060417/ED)

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http://www.cas.org/infopolicy.html

=> s cofilin
777 COFILIN
232 COFILINS
L1 814 COFILIN
(COFILIN OR COFILINS)

=> s inhibit?
L2 1822517 INHIBIT?

=> s l1 (L) l2
L3 221 L1 (L) L2

=> s hepatocar? or mesenchy? or nuroectoder? or (ewing?)
7077 HEPATOCAR?
15151 MESENCHY?
0 NUROECTODER?
1659 EWING?

```
L4       23829 HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)

=> s l3 and l4
L5           1 L3 AND L4

=> d ibib

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2002:977858  CAPLUS
DOCUMENT NUMBER:          138:52333
TITLE:                    Pharmaceutical composition for diagnosis, prevention
                          or treatment of a tumorous state, comprising a
                          modulator of the actin polymerization state
INVENTOR(S):              Auclair, Christian; Amsellem, Valerie; Hervy, Martial;
                          Subra, Frederic
PATENT ASSIGNEE(S):       Bioalliance Pharma, Fr.; Ecole Normale Superieure De
                          Cachan; Institut Gustave Roussy-IGR; Centre National
                          de la Recherche Scientifique CNRS
SOURCE:                   PCT Int. Appl., 68 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2002102846         A2    20021227    WO 2002-FR2106           20020618
     WO 2002102846         A3    20040422
     WO 2002102846         B1    20040603
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
             GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
             GN, GQ, GW, ML, MR, NE, SN, TD, TG
     FR 2825928            A1    20021220    FR 2001-7976             20010618
     FR 2825928            B1    20040402
     CA 2450845            AA    20021227    CA 2002-2450845          20020618
     EP 1432732            A2    20040630    EP 2002-745538           20020618
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2005504521         T2    20050217    JP 2003-506318           20020618
     US 2004191230         A1    20040930    US 2003-740266           20031218
PRIORITY APPLN. INFO.:                       FR 2001-7976         A   20010618
                                             WO 2002-FR2106       W   20020618


=> s actin
         49687 ACTIN
         30340 ACTINS
L6       52687 ACTIN
               (ACTIN OR ACTINS)

=> s stabil?
L7     1026058 STABIL?

=> s l6 (l) l7
L8        2489 L6 (L) L7

=> d his
```

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     (FILE 'HOME' ENTERED AT 09:03:09 ON 18 APR 2006)

     FILE 'CAPLUS' ENTERED AT 09:03:17 ON 18 APR 2006
L1           814 S COFILIN
L2       1822517 S INHIBIT?
L3           221 S L1 (L) L2
L4         23829 S HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)
L5             1 S L3 AND L4
L6         52687 S ACTIN
L7       1026058 S STABIL?
L8          2489 S L6 (L) L7

=> s l8 and l4
L9           19 L8 AND L4

=> s l9 not py>2002
       3759065 PY>2002
L10           8 L9 NOT PY>2002

=> s l9 not py>2001
       4742175 PY>2001
L11           8 L9 NOT PY>2001

=> d ibib 1-8

L11  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2002:88952  CAPLUS
DOCUMENT NUMBER:          136:242165
TITLE:                    TGFβ is required for the formation of
                          capillary-like structures in three-dimensional
                          cocultures of 10T1/2 and endothelial cells
AUTHOR(S):                Darland, D. C.; D'Amore, P. A.
CORPORATE SOURCE:         The Schepens Eye Research Institute and the Department
                          of Ophthalmology, Harvard Medical School, Boston, MA,
                          02114, USA
SOURCE:                   Angiogenesis (2001), 4(1), 11-20
                          CODEN: AGIOFT; ISSN: 0969-6970
PUBLISHER:                Kluwer Academic Publishers
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          51    THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11  ANSWER 2 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2001:7412  CAPLUS
DOCUMENT NUMBER:          134:264229
TITLE:                    Integrin α3β1 engagement disrupts
                          intercellular adhesion
AUTHOR(S):                Kawano, Kenji; Kantak, Seema S.; Murai, Mutsuhiko;
                          Yao, Chung-Chen; Kramer, Randall H.
CORPORATE SOURCE:         Department of Stomatology, University of California at
                          San Francisco, San Francisco, CA, 94143-0512, USA
SOURCE:                   Experimental Cell Research (2001), 262(2), 180-196
                          CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER:                Academic Press
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          66    THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11  ANSWER 3 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2000:336418  CAPLUS
DOCUMENT NUMBER:          133:87270
TITLE:                    The tetraspan molecule CD151, a novel constituent of
```

hemidesmosomes, associates with the integrin α6β4 and may regulate the spatial organization of hemidesmosomes
AUTHOR(S): Sterk, Lotus M. Th.; Geuijen, Cecile A. W.; Oomen, Lauran C. J. M.; Calafat, Jero; Janssen, Hans; Sonnenberg, Arnoud
CORPORATE SOURCE: Division of Cell Biology, The Netherlands Cancer Institute, Amsterdam, 1066 CX, Neth.
SOURCE: Journal of Cell Biology (2000), 149(4), 969-982
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:517212 CAPLUS
DOCUMENT NUMBER: 129:170359
TITLE: Expression of human bone morphogenic protein 7 in primary rabbit periosteal cells. Potential utility in gene therapy for osteochondral repair
AUTHOR(S): Mason, J. M.; Grande, D. A.; Barcia, M.; Grant, R.; Pergolizzi, R. G.; Breitbart, A. S.
CORPORATE SOURCE: Viral Vector Lab., Dep. Res., North Shore Univ. Hosp.-New York Univ. Sch. Med., Manhasset, NY, 11030, USA
SOURCE: Gene Therapy (1998), 5(8), 1098-1104
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:269919 CAPLUS
DOCUMENT NUMBER: 126:260361
TITLE: Modulation of LDL receptor mRNA stability by phorbol esters in human liver cell culture models
AUTHOR(S): Wilson, G. M.; Roberts, E. A.; Deeley, R. G.
CORPORATE SOURCE: Department of Biochemistry and Cancer Research Laboratories, Queen's University, Kingston, ON, Can.
SOURCE: Journal of Lipid Research (1997), 38(3), 437-446
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:145098 CAPLUS
DOCUMENT NUMBER: 116:145098
TITLE: Gene regulatory factors of the sea urchin embryo. I. Purification by affinity chromatography and cloning of P3A2, a novel DNA-binding protein
AUTHOR(S): Calzone, Frank J.; Hoeoeg, Christer; Teplow, David B.; Cutting, Ann E.; Zeller, Robert W.; Britten, Roy J.; Davidson, Eric H.
CORPORATE SOURCE: Div. Biol., California Inst. Technol., Pasadena, CA, 91125, USA
SOURCE: Development (Cambridge, United Kingdom) (1991), 112(1), 335-50
CODEN: DEVPED; ISSN: 0950-1991

DOCUMENT TYPE: Journal
LANGUAGE: English

L11 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:595544 CAPLUS
DOCUMENT NUMBER: 107:195544
TITLE: Developmental and tissue-specific regulation of β-tubulin gene expression in the embryo of the sea urchin Strongylocentrotus purpuratus
AUTHOR(S): Harlow, Patricia; Nemer, Martin
CORPORATE SOURCE: Inst. Cancer Res., Fox Chase Cancer Cent., Philadelphia, PA, 19111, USA
SOURCE: Genes & Development (1987), 1(2), 147-60
CODEN: GEDEEP; ISSN: 0890-9369
DOCUMENT TYPE: Journal
LANGUAGE: English

L11 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:140906 CAPLUS
DOCUMENT NUMBER: 98:140906
TITLE: A yellow crescent cytoskeletal domain in ascidian eggs and its role in early development
AUTHOR(S): Jeffery, William R.; Meier, Stephen
CORPORATE SOURCE: Dep. Zool., Univ. Texas, Austin, TX, 78712, USA
SOURCE: Developmental Biology (Orlando, FL, United States) (1983), 96(1), 125-43
CODEN: DEBIAO; ISSN: 0012-1606
DOCUMENT TYPE: Journal
LANGUAGE: English

=> d kwic 3

L11 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AB . . . and certain integrins to form large complexes at the cell surface. CD151 is expressed by a variety of epithelia and mesenchymal cells. We demonstrate here that in human skin CD151 is codistributed with α3β1 and α6β4 at the basolateral surface of. . . cell surface in association with patches of laminin-5. Focal adhesions are present at the periphery of these clusters, connected with actin filaments, and they contain both CD151 and α3β1. Transient transfection studies of PA-JEB cells with β4 revealed that the integrin. . . recruitment into hemidesmosomes is regulated by the integrin α6β4. We suggest that CD151 plays a role in the formation and stability of hemidesmosomes by providing a framework for the spatial organization of the different hemidesmosomal components.

=> s dolastatin or jasplakinolide
390 DOLASTATIN
59 DOLASTATINS
404 DOLASTATIN
(DOLASTATIN OR DOLASTATINS)
251 JASPLAKINOLIDE
1 JASPLAKINOLIDES
252 JASPLAKINOLIDE
(JASPLAKINOLIDE OR JASPLAKINOLIDES)
L12 652 DOLASTATIN OR JASPLAKINOLIDE

=> d his

(FILE 'HOME' ENTERED AT 09:03:09 ON 18 APR 2006)

FILE 'CAPLUS' ENTERED AT 09:03:17 ON 18 APR 2006

```
L1          814 S COFILIN
L2      1822517 S INHIBIT?
L3          221 S L1 (L) L2
L4        23829 S HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)
L5            1 S L3 AND L4
L6        52687 S ACTIN
L7      1026058 S STABIL?
L8         2489 S L6 (L) L7
L9           19 S L8 AND L4
L10           8 S L9 NOT PY>2002
L11           8 S L9 NOT PY>2001
L12         652 S DOLASTATIN OR JASPLAKINOLIDE

=> s l12 and l4
L13           8 L12 AND L4

=> s l13 not py>2001
       4742175 PY>2001
L14           0 L13 NOT PY>2001

=> s l13 not py>2002
       3759065 PY>2002
L15           0 L13 NOT PY>2002

=> d l13 ibib 1-8

L13  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2006:13464  CAPLUS
DOCUMENT NUMBER:          144:101073
TITLE:                    therapeutic uses of kinase inhibitors, and
                          compositions thereof
INVENTOR(S):              Caligiuri, Maureen G.; Kley, Nikolai A.; Murthi,
                          Krishna K.
PATENT ASSIGNEE(S):       GPC Biotech, Inc., USA
SOURCE:                   PCT Int. Appl., 201 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2006002119         A2    20060105    WO 2005-US21843         20050617
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM,
             KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG,
             KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                        US 2004-580868P     P  20040618
OTHER SOURCE(S):          MARPAT 144:101073

L13  ANSWER 2 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:1290072  CAPLUS
DOCUMENT NUMBER:          144:46998
TITLE:                    The X-ray crystal structure of BRCA1 tandem BRCT
                          repeat and BACH1 phosphopeptide complex and methods
                          and compositions for antitumor drug design
```

INVENTOR(S): Yaffe, Michael B.; Clapperton, Julie A.; Manke, Isaac A.; Lowery, Drew M.; Ho, Timmy; Haire, Lesley F.; Smerdon, Stephen J.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 360 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005115454	A2	20051208	WO 2005-US15981	20050509

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-569131P P 20040507

L13 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409543 CAPLUS
DOCUMENT NUMBER: 142:457053
TITLE: Human protein IAP (inhibitor of apoptosis protein) nucleobase oligomers, including dsRNA, shRNA, and siRNA, and their use for enhancing apoptosis in cancer therapy
INVENTOR(S): Lacasse, Eric; McManus, Daniel
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042558	A1	20050512	WO 2004-CA1902	20041029

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005148535	A1	20050707	US 2004-975974	20041028

PRIORITY APPLN. INFO.: US 2003-516192P P 20031030

L13 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409357 CAPLUS
DOCUMENT NUMBER: 142:457052
TITLE: Sequences of antisense IAP (inhibitor of apoptosis

protein) oligomers and their use for treatment of proliferative diseases with a chemotherapeutic agent
INVENTOR(S): Lacasse, Eric; McManus, Daniel; Durkin, Jon P.
PATENT ASSIGNEE(S): Aegera Therapeutics, Inc., Can.
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042030	A1	20050512	WO 2004-CA1900	20041029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005119217	A1	20050602	US 2004-975790	20041028

PRIORITY APPLN. INFO.: US 2003-516263P P 20031030
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:283298 CAPLUS
DOCUMENT NUMBER: 142:349042
TITLE: Combinations of chlorpromazine compounds and antiproliferative drugs for the treatment of neoplasms
INVENTOR(S): Lee, Margaret S.; Nichols, James M.; Zhang, Yanzhen; Keith, Curtis
PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005027842	A2	20050331	WO 2004-US30368	20040916
WO 2005027842	A3	20051222		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2003-504310P P 20030918
OTHER SOURCE(S): MARPAT 142:349042

L13 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:248055 CAPLUS

DOCUMENT NUMBER: 142:352644
TITLE: RhoA/ROCK Signaling Regulates Sox9 Expression and Actin Organization during Chondrogenesis
AUTHOR(S): Woods, Anita; Wang, Guoyan; Beier, Frank
CORPORATE SOURCE: Canadian Institutes of Health Research Group in Skeletal Development and Remodeling, Department of Physiology and Pharmacology, University of Western Ontario, London, ON, N6A 5C1, Can.
SOURCE: Journal of Biological Chemistry (2005), 280(12), 11626-11634
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 73 THERE ARE 73 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:816528 CAPLUS
DOCUMENT NUMBER: 140:12638
TITLE: Two CD95 tumor classes with different sensitivities to antitumor drugs
AUTHOR(S): Algeciras-Schimnich, Alicia; Pietras, Eric M.; Barnhart, Bryan C.; Legembre, Patrick; Vijayan, Shrijay; Holbeck, Susan L.; Peter, Marcus E.
CORPORATE SOURCE: The Ben May Institute for Cancer Research, University of Chicago, Chicago, IL, 60637, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(20), 11445-11450
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:924095 CAPLUS
DOCUMENT NUMBER: 136:31647
TITLE: Toxicity typing using mesenchymal stem cells
INVENTOR(S): Snodgrass, H. Ralph
PATENT ASSIGNEE(S): Vistagen, Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096865	A1	20011220	WO 2001-US19048	20010614
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2412769	AA	20011220	CA 2001-2412769	20010614
US 2002045179	A1	20020418	US 2001-881475	20010614
EP 1290443	A1	20030312	EP 2001-946335	20010614

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        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004503255        T2    20040205    JP 2002-510943          20010614
PRIORITY APPLN. INFO.:                      US 2000-211608P     P   20000614
                                            WO 2001-US19048     W   20010614
REFERENCE COUNT:         7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> file pctfull
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    51.50      51.71

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -0.75      -0.75

FILE 'PCTFULL' ENTERED AT 09:07:34 ON 18 APR 2006
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FILE LAST UPDATED:         11 APR 2006      <20060411/UP>
MOST RECENT UPDATE WEEK:       200614        <200614/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
    SEE
    http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE
    (last updated April 10, 2006) <<<

=> s dolastatin or jasplakinolide
           459 DOLASTATIN
            70 DOLASTATINS
           477 DOLASTATIN
                 (DOLASTATIN OR DOLASTATINS)
           171 JASPLAKINOLIDE
             1 JASPLAKINOLIDES
           171 JASPLAKINOLIDE
                 (JASPLAKINOLIDE OR JASPLAKINOLIDES)
L16        643 DOLASTATIN OR JASPLAKINOLIDE

=> s hepatocar? or mesenchy? or nuroectoder? or (ewing?)
           770 HEPATOCAR?
          5688 MESENCHY?
             0 NUROECTODER?
          3185 EWING?
L17       8782 HEPATOCAR? OR MESENCHY? OR NUROECTODER? OR (EWING?)

=> s l17 and l16
L18        243 L17 AND L16

=> s l18 not py>2001
        488865 PY>2001
L19         16 L18 NOT PY>2001

=> s l16/clm
            60 DOLASTATIN/CLM
             7 JASPLAKINOLIDE/CLM
L20         67 (DOLASTATIN/CLM OR JASPLAKINOLIDE/CLM)

=> s l20 and l19
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L21          0 L20 AND L19

=> s l19 not py>2000
        587352 PY>2000
L22          8 L19 NOT PY>2000

=> d ibib 1-8

L22    ANSWER 1 OF 8     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2000071135 PCTFULL  ED 20020515
TITLE (ENGLISH):         ANTI-TUMOR COMPRISING BOROPROLINE COMPOUNDS
TITLE (FRENCH):          AGENTS ANTI-TUMORALES CONTENANT DES COMPOSES DE
                         BOROPROLINE
INVENTOR(S):             WALLNER, Barbara, P.;
                         MILLER, Glenn
PATENT ASSIGNEE(S):      POINT THERAPEUTICS, INC.
LANGUAGE OF PUBL.:       English
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 2000071135         A1 20001130
DESIGNATED STATES
       W:                AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ
                         DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
                         JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
                         MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
                         TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ
                         TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK
                         ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM
                         GA GN GW ML MR NE SN TD TG
APPLICATION INFO.:       WO 2000-US14505       A  20000525
PRIORITY INFO.:          US 1999-60/135,861       19990525

L22    ANSWER 2 OF 8     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        2000067802 PCTFULL  ED 20020515
TITLE (ENGLISH):         FATTY ACID-N-SUBSTITUTED INDOL-3-GLYOXYL-AMIDE
                         COMPOSITIONS AND USES THEREOF
TITLE (FRENCH):          COMPOSITIONS D'ACIDES GRAS -N-SUBSTITUTED
                         INDOL-3-GLYOXYL-AMIDE ET LEUR UTILISATION
INVENTOR(S):             BRADLEY, Matthews, O.;
                         SWINDELL, Charles, S.;
                         ANTHONY, Forrest;
                         WEBB, Nigel, L.;
                         FISHER, Mark
PATENT ASSIGNEE(S):      PROTARGA, INC.
LANGUAGE OF PUBL.:       English
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 2000067802         A1 20001116
DESIGNATED STATES
       W:                AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ
                         DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
                         JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
                         MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
                         TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG
                         ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI
                         FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN
                         GW ML MR NE SN TD TG
APPLICATION INFO.:       WO 2000-US12752       A  20000510
PRIORITY INFO.:          US 1999-60/133,292       19990510

L22    ANSWER 3 OF 8     PCTFULL   COPYRIGHT 2006 Univentio on STN
```

ACCESSION NUMBER: 2000064946 PCTFULL ED 20020515
TITLE (ENGLISH): COMPOSITIONS AND METHODS FOR CANCER TREATMENT BY SELECTIVELY INHIBITING VEGF
TITLE (FRENCH): COMPOSITIONS ET PROCEDES DE TRAITEMENT DU CANCER PAR INHIBITION SELECTIVE DE VEGF
INVENTOR(S): THORPE, Philip, E.;
BREKKEN, Rolf, A.
PATENT ASSIGNEE(S): BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000064946	A2	20001102

DESIGNATED STATES
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2000-US11367 A 20000428
PRIORITY INFO.: US 1999-60/131,432 19990428

L22 ANSWER 4 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2000050016 PCTFULL ED 20020515
TITLE (ENGLISH): COMPOSITIONS AND METHODS FOR IMPROVING INTEGRITY OF COMPROMISED BODY PASSAGEWAYS AND CAVITIES
TITLE (FRENCH): COMPOSITIONS ET METHODES POUR L'AMELIORATION DE L'INTEGRITE DE CAVITES ET DE PASSAGES CORPORELS AFFAIBLIS
INVENTOR(S): SIGNORE, Pierre, E.;
MACHAN, Lindsay, S.
PATENT ASSIGNEE(S): ANGIOTECH PHARMACEUTICALS, INC.;
SIGNORE, Pierre, E.;
MACHAN, Lindsay, S.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000050016	A2	20000831

DESIGNATED STATES
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2000-CA175 A 20000223
PRIORITY INFO.: US 1999-60/121,424 19990223

L22 ANSWER 5 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999062510 PCTFULL ED 20020515
TITLE (ENGLISH): COMPOSITIONS COMPRISING ANTI-MICROTUBULE AGENTS FOR TREATING OR PREVENTING INFLAMMATORY DISEASES
TITLE (FRENCH): COMPOSITIONS RENFERMANT DES AGENTS ANTI-MICROTUBULES POUR LE TRAITEMENT OU LA PREVENTION DE MALADIES INFLAMMATOIRES
INVENTOR(S): HUNTER, William, L.
PATENT ASSIGNEE(S): ANGIOTECH PHARMACEUTICALS, INC.;

HUNTER, William, L.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9962510	A2	19991209

DESIGNATED STATES
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 1999-CA464 A 19990601
PRIORITY INFO.: US 1998-09/088,546 19980601

L22 ANSWER 6 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999055343 PCTFULL ED 20020515
TITLE (ENGLISH): CNRE BINDING FACTORS AND USES THEREOF
TITLE (FRENCH): FACTEURS DE LIAISON CNRE ET UTILISATIONS CORRESPONDANTES
INVENTOR(S): CHEN, Yuqing, E.;
HORIUCHI, Masatsugu;
DZAU, Victor, J.;
TAMURA, Koichi
PATENT ASSIGNEE(S): THE BRIGHAM AND WOMEN'S HOSPITAL, INC.;
CHEN, Yuqing, E.;
HORIUCHI, Masatsugu;
DZAU, Victor, J.;
TAMURA, Koichi
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9955343	A1	19991104

DESIGNATED STATES
W: CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.: WO 1999-US8502 A 19990423
PRIORITY INFO.: US 1998-60/082,997 19980424

L22 ANSWER 7 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1999004817 PCTFULL ED 20020515
TITLE (ENGLISH): CHEMOTHERAPY SYNERGISTIC AGENT
TITLE (FRENCH): AGENT SYNERGIQUE POUR CHIMIOTHERAPIE
INVENTOR(S): WINKELMAN, James, W.;
BRIDGES, Kenneth, R.
PATENT ASSIGNEE(S): BRIGHAM & WOMEN'S HOSPITAL, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9904817	A1	19990204

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.: WO 1998-US15052 A 19980722
PRIORITY INFO.: US 1997-60/053,696 19970725
US 1997-60/054,148 19970725

L22 ANSWER 8 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 1998035554 PCTFULL ED 20020514
TITLE (ENGLISH): COMBINED TUMOR SUPPRESSOR GENE THERAPY AND CHEMOTHERAPY IN THE TREATMENT OF NEOPLASMS
TITLE (FRENCH): COMBINAISON THERAPIE GENIQUE SUPPRESSIVE DE TUMEURS - CHIMIOTHERAPIE UTILISEE DANS LE TRAITEMENT DE NEOPLASMES
INVENTOR(S): NIELSEN, Loretta;
HOROWITZ, Jo, Ann;
MANEVAL, Daniel, C.;
DEMERS, G., William;
RYBAK, Mary, Ellen;
RESNICK, Gene
PATENT ASSIGNEE(S): CANJI, INC.;
NIELSEN, Loretta;
HOROWITZ, Jo, Ann;
MANEVAL, Daniel, C.;
DEMERS, G., William;
RYBAK, Mary, Ellen;
RESNICK, Gene
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9835554	A2	19980820

DESIGNATED STATES
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1998-US3514	A	19980217
PRIORITY INFO.:	US 1997-8/801,285		19970218
	US 1997-8/801,681		19970218
	US 1997-8/801,755		19970218
	US 1997-8/801,765		19970218
	US 1997-60/038,065		19970218
	US 1997-60/047,834		19970528

=> d kwic 5, 7

L22 ANSWER 5 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . subtilisin, 1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol, flavanol, rotenone, griseofulvin, vinca alkaloids, including
vinblastine and vincristine, maytansinoids and ansamitocins, rhizoxin, phornopsin A,
ustiloxins, dolastatin 10, dolastatin 15,
halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam. betaine. taurine, isethionate, HO-221, adociasulfate-2,
estramustine, monoclonal anti-idiotypic antibodies, microtubule assembly promoting
protein (taxol-like protein, TALP),. . .
. . .
phomopsin A (Hamel, Med. Res. Rev. 16(2): 207-23) 1, 1996), ustiloxins (Hamel, Med Res. Rev. 16(2): 207-23) 1, 1996), dolastatin I 0 (Hamel, Med. Res. Rev.

16(2): 207-23) 1, 1996). dolastatin 15 (Hamel. Med Res. Rev.

16(2): 207-23) 1, 1996),
halichondrins and halistatins (Hamel, Med. Res. Rev. 16(2): 207-231, 1996),
spongistatins (Hamel,. . .
. . .
subtilisin,
1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol, flavanol,
rotenone, griseofulvin, vinca alkaloids, including vinblastine and vincristine,
maytansinoids and ansamitocins, rhizoxin. phomopsin A. ustiloxins,
dolastatin 10,
dolastatin 15, halichondrins and halistatins, spongistatins.
cryptophycins, rhazinilam,
betaine, taurine, isethionate. HO-221, adociasulfate-2, estramustine.
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein
(taxol-like. . .
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subtilisin,
1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxvestradiol, flavanol,
rotenone, griseofulvin, vinca alkaloids, including vinblastine and vincristine,
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dolastatin I 0,
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subtilisin,
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dolastatin 10,
dolastatin 15. halichondrins and halistatins, spongistatins,
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idiotypic antibodies, microtubule assembly promoting protein
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dolastatin 10.

dolastatin 15, halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam,
betaine, taurine, isethionate, HO-221, adociasulfate-2, estramustine,
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein
(taxol-like. . .
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subtilisin. 1069C85, steganacin,
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rotenone, griseofulvin,

vinca alkaloids. including vinblastine and vincristine, maytansinoids and ansamitocins,
rhizoxin, phomopsin A. ustiloxins, dolastatin 10.
dolastatin 15, halichondrins and
halistatins, spongistatins, cryptophycins, rhazinilam, betaine, taurine.
isethionate, HO-
221, adociasulfate-2, estramustine. monoclonal anti-idiotypic
antibodies. microtubule
assembly promoting protein (taxol-like protein,. . .

maytansinoids and ansainitocins, rhizoxin. phomopsin A, ustiloxins,
dolastatin I 0,
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cryptophycins. rhazinilam,
betaine, taurine, isethionate, HO-22 1, adociasulfate-2, estraniustine,
monoclonal anti-
idiotypic antibodies, microtubule assembly promoting protein. . .
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1069C85, steganacin, combretastatin, curacin, estradiol,
2-methoxyestradiol. flavanol,
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dolastatin 15, halichondrins and halistatins, spongistatins,
cryptophycins, rhazinilam,
betaine. taurine. isethionate, HO-221, adociasulfate-2, estramustine,
microtubule
assembly promoting protein (taxol-like protein, TALP), cell swelling. .
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subtilisin,
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2-methoxyestradiol. flavanol,
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cryptophycins, rhazinilam, betaine, taurine, isethionate, HO-221,
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estramustine, monoclonal anti-idiotypic antibodies, microtubule assembly
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adociasulfate
estramustine, monoclonal anti-idiotypic antibodies, microtubule assembly
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phomopsin A,
ustiloxins, dolastatin 10, dolastatin 15,
halichondrins and halistatins. spongistatins.
. . .
endpoints: (1) inhibition of
the white blood cell response (macrophages, neutrophils and T cells)
which initiates the
inflammatory cascade; (2) inhibition of mesenchyrnal cell
(fibroblasts, synoviocytes,
etc.) hyperproliferation that leads to the development of fibrosis and
loss of organ
function; (3) inhibition of matrix metalloproteinase. . .

L22 ANSWER 7 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . 91)
-
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous
cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal
cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal
cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcorna and
osteosarcoma; skin

cancer, including melanoma, Kaposi's sarcoma, basal. . .
. . .
peptides; insulin-like
growth factor-I receptor inhibitor; interferon agonists; interferons;
interleukins; iobenguane;
I 0 iododoxorubicin; ipomeanol, 4-; irinotecan; iroplact; irsogladine;
isobengazole;
isohomohalicondrin B; itasetron; jasplakinolide; kahalalide F;
larnellarin-N triacetate;
lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin;
letrozole; leukemia
inhibiting factor; leukocyte alpha interferon; leuprolide + estrogen +
progesterone;
leuprorelin;. . .

CLMEN. . . and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous
cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal
cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal
cancer; sarcomas, including
leiornyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and
osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basocellular. . .
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and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squarnous
cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal
cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer; rectal
cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and
osteosarcoma; skin
- 24 -
cancer, including melanoma, Kaposi's. . .
. . .
and
lymphocytic lymphomas; neuroblastomas; oral cancer, including squamous
cell carcinoma;
ovarian cancer, including those arising from epithelial cells, stromal
cells, germ cells and
mesenchymal cells; pancreas cancer; prostate cancer'; rectal
cancer; sarcomas, including
leiomyosarcoma, rhabdomyosarcoma, liposarcoma, fibrosarcoma and
osteosarcoma; skin
cancer, including melanoma, Kaposi's sarcoma, basocellular. . .

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 8	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 13	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 14	DEC 18	CA/CAplus patent kind codes updated
NEWS 15	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 17	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 23	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 24	JAN 29	PHAR reloaded with new search and display fields
NEWS 25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 26	FEB 13	CASREACT coverage to be extended
NEWS 27	Feb 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 28	Feb 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 29	Feb 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 30	Feb 26	MEDLINE reloaded with enhancements
NEWS 31	Feb 26	EMBASE enhanced with Clinical Trial Number field
NEWS 32	Feb 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 33	Feb 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 34	Feb 26	CAS Registry Number crossover limit increased from 10,000

to 300,000 in multiple databases

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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=> s ESP-2 or HED-2 or Zyxin or Zyxin-2
511000 ESP
263 ESPS
511131 ESP
(ESP OR ESPS)
9071127 2
958 ESP-2
(ESP(W)2)
397 HED
35 HEDS
428 HED
(HED OR HEDS)

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        9071127 2
              5 HED-2
                  (HED(W)2)
            249 ZYXIN
             28 ZYXINS
            254 ZYXIN
                  (ZYXIN OR ZYXINS)
            249 ZYXIN
             28 ZYXINS
            254 ZYXIN
                  (ZYXIN OR ZYXINS)
        9071127 2
              6 ZYXIN-2
                  (ZYXIN(W)2)
L1          1213 ESP-2 OR HED-2 OR ZYXIN OR ZYXIN-2

=> s cancer? or tumor? or neoplas?
          323384 CANCER?
          460516 TUMOR?
          483669 NEOPLAS?
L2        763127 CANCER? OR TUMOR? OR NEOPLAS?

=> s l1 (L) l2
L3            73 L1 (L) L2

=> s therap? or treat? or inhibit? or suppres?
          509077 THERAP?
         3519011 TREAT?
         1906473 INHIBIT?
          411937 SUPPRES?
L4       5345131 THERAP? OR TREAT? OR INHIBIT? OR SUPPRES?
 75% OF LIMIT FOR TOTAL ANSWERS REACHED

=> s l4 and l3
L5            55 L4 AND L3

=> s l5 not py>2000
        6894468 PY>2000
L6            14 L5 NOT PY>2000

=> d ibib abs 1-7

L6   ANSWER 1 OF 14  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2000:738475  CAPLUS
DOCUMENT NUMBER:          134:220517
TITLE:                    Alterations in the gene expression profile of MCF-7
                          breast tumor cells in response to c-Jun
AUTHOR(S):                Rinehart-Kim, Janet; Johnston, Melissa; Birrer,
                          Michael; Bos, Timothy
CORPORATE SOURCE:         Department of Microbiology and Molecular Cell Biology,
                          Eastern Virginia Medical School, Norfolk, VA, USA
SOURCE:                   International Journal of Cancer (2000), 88(2), 180-190
                          CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER:                Wiley-Liss, Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   MCF7 breast tumor cells overexpressing human c-Jun exhibit a transformed
     phenotype characterized not only by increased tumorigenicity but also by
     enhanced motility and invasion.  The cellular phenotypic response to c-Jun
     overexpression is likely due, at least in part, to altered patterns of
     gene expression.  In order to begin to understand the complexities by
     which elevated production of c-Jun alters the state of the cell, the authors
     have profiled the expression of 588 different genes by comparative
     hybridization.  By using this approach, the authors have identified a
     total of 21 upregulated or downregulated gene targets responsive to c-Jun
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overexpression. Interestingly, 8 of these genes have been previously found associated with c-Jun or AP-I activity and therefore provide internal validation for this approach to target gene discovery. The remaining 13 genes represent potential new c-Jun regulated target genes. Genomic sequence information was available for 15 of the 21 genes identified in this screen. Anal. of these genomic sequences revealed the presence of AP-I or AP-I-like sequences in 12 of the 15 genes examined Consistent with a direct mechanism of target regulation by c-Jun, gel shift anal. of selected AP-I-containing promoter regions revealed elevated and specific binding by proteins present in nuclear exts. of c-Jun expressing MCF7 cells.

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:734436 CAPLUS
DOCUMENT NUMBER: 134:14198
TITLE: Differential display analysis of fiber-induced carcinogenesis in rat: clue for involvement of integrin-mediated signal transduction
AUTHOR(S): Sandhu, H.; Olbruck, H.; Abel, J.; Unfried, K.
CORPORATE SOURCE: Department of Experimental Toxicology, Medical Institute of Environmental Hygiene at the Heinrich Heine University, Dusseldorf, 40225, Germany
SOURCE: Inhalation Toxicology (2000), 12(Suppl. 3), 337-343
CODEN: INHTE5; ISSN: 0895-8378
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this study, mRNA expression patterns during mesothelioma carcinogenesis in the peritoneal cavity were investigated. To this purpose, the mRNA expression patterns of fiber-induced mesothelioma and of fiber-treated tissues were compared to untreated tissues, resp. Suppression subtractive hybridization (SSH) and an array hybridization assay were used to perform differential display analyses. Genes found to be expressed differentially mainly represent proteins of signal transduction pathways and regulatory proteins of the cell cycle. The genes for components of the AP-1 transcription factor, c-jun, c-fos, and fra-1 (fos-related antigen-1) are upregulated in nontumorous tissue treated with asbestos. These data confirm in vivo the involvement of AP-1 expression as response to fiber treatment. In addition, osteopontin, zyxin, and integrin-linked kinase were upregulated in tumors and in treated tissues. These genes code for proteins involved in the signal transduction from the extracellular matrix to the nucleus. Using integrin-specific inhibitors, the apoptotic effects of crocidolite fibers could be suppressed significantly. From these results the authors hypothesize that direct effects of the fibers on the target tissue are mediated by interaction of the fibers with the extracellular matrix mols.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:727041 CAPLUS
DOCUMENT NUMBER: 134:81
TITLE: Preparation of novel specific aminopeptidase inhibitors with a cyclic imide skeleton
AUTHOR(S): Takahashi, Hiroyasu; Komoda, Masato; Katsuta, Hiroki; Hashimoto, Yuichi
CORPORATE SOURCE: Institute of Molecular and Cellular Bioscience, University of Tokyo, Tokyo, 113-0032, Japan
SOURCE: Yakugaku Zasshi (2000), 120(10), 909-922
CODEN: YKKZAJ; ISSN: 0031-6903
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review with 25 refs. The studies on both structure-activity relationship study and identification of the target enzyme of novel nonpeptide aminopeptidase inhibitors with cyclic imide skeleton are reviewed. Some N-phenylphthalimide or N-phenylhomophthalimide derivative showed potent protease inhibitory activity in an assay system using human acute lymphoblastic leukemia cells, Molt-4, with alanine-4-methylcoumaryl-7-amide (ala-AMC) as a substrate. Esp ., 2-(2,6-diethylphenyl)-1,2,3,4-tetrahydroisoquinoline-1,3-dione (PIQ-22) (3) was found to be the most potent inhibitor and further it showed potent tumor-cell invasion inhibitory activity that is more effective than potent peptide aminopeptidase inhibitors such as bestatin (1) or actinonin (2). For the further investigation of this novel protease inhibitory activity, we have carried out the structural development of PIQ-22 (3) and it is assumed that tautomerism of imidobenzoylketone in cyclic imide structure may be related to the inhibitory activity. The requirement for the activity of electron donating groups such as NH2 or OH to the condensed Ph ring in phthalimide inhibitors also supports this possibility. The target aminopeptidase of PIQ-22 was identified as puromycin-sensitive aminopeptidase (PSA), by N-terminal amino acid sequencing, and by comparison with chromatog. behavior and substrate-selectivity, and so on. Lineweaver-Burk plot showed that PSA is inhibited by PIQ-22 (3) in a noncompetitive manner while puromycin (83) and bestatin (1) inhibit PSA competitively.

L6 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:393023 CAPLUS

DOCUMENT NUMBER: 133:117982

TITLE: Zyxin, a regulator of actin filament assembly, targets the mitotic apparatus by interacting with h-warts/LATS1 tumor suppressor

AUTHOR(S): Hirota, Toru; Morisaki, Tetsuro; Nishiyama, Yasuyuki; Marumoto, Tomotoshi; Tada, Kenji; Hara, Toshihiro; Masuko, Norio; Inagaki, Masaki; Hatakeyama, Katsuyoshi; Saya, Hideyuki

CORPORATE SOURCE: Department of Tumor Genetics and Biology, Kumamoto University School of Medicine, Kumamoto, 860-0811, Japan

SOURCE: Journal of Cell Biology (2000), 149(5), 1073-1086
CODEN: JCLBA3; ISSN: 0021-9525

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The mitotic apparatus plays a pivotal role in dividing cells to ensure each daughter cell receives a full set of chromosomes and complement of cytoplasm during mitosis. A human homolog of the Drosophila warts tumor suppressor, h-warts/LATS1, is an evolutionarily conserved serine/threonine kinase and a dynamic component of the mitotic apparatus We have identified an interaction of h-warts/LATS1 with zyxin, a regulator of actin filament assembly. Zyxin is a component of focal adhesion; however, during mitosis, a fraction of cytoplasmic-dispersed zyxin becomes associated with h-warts/LATS1 on the mitotic apparatus We found that zyxin is phosphorylated specifically during mitosis, most likely by Cdc2 kinase, and that the phosphorylation regulates association with h-warts/LATS1. Furthermore, microinjection of truncated h-warts/LATS1 protein, including the zyxin-binding portion, interfered with localization of zyxin to mitotic apparatus, and the duration of mitosis of these injected cells was significantly longer than that of control cells. These findings suggest that h-warts/LATS1 and zyxin play a crucial role in controlling mitosis progression by forming a regulatory complex on mitotic apparatus

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:358265 CAPLUS
DOCUMENT NUMBER: 133:100802
TITLE: mRNA expression patterns in different stages of asbestos-induced carcinogenesis in rats
AUTHOR(S): Sandhu, H.; Dehnen, W.; Roller, M.; Abel, J.; Unfried, K.
CORPORATE SOURCE: Department of Experimental Toxicology, Medical Institute of Environmental Hygiene at the Heinrich Heine University, Dusseldorf, 40225, Germany
SOURCE: Carcinogenesis (2000), 21(5), 1023-1029
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human malignant mesotheliomas are induced almost exclusively by fibrous dusts. The nature of interactions between fibers and target cells, and the mol. mechanisms leading to tumorigenesis, are not yet understood. Here, the mRNA expression patterns at different stages of asbestos-induced carcinogenesis in rats were monitored by suppression subtractive hybridization (SSH) and array assay. Several genes were upregulated in pre-tumorous tissues from asbestos-treated rats, in asbestos-induced tumors, and in cells treated with asbestos in vitro. The upregulation of the proto-oncogene c-myc, fra-1, and egfr in fiber-induced carcinogenesis was demonstrated at different stages of carcinogenesis. A possible role of Fra-1 as one of the dimeric proteins generating the AP-1 transcription factor was substantiated by its dose-dependent expression in mesothelial cells treated with asbestos in vitro. The upregulation of osteopontin (an extracellular matrix protein) and of zyxin and integrin-linked kinase (intracellular proteins associated with the focal adhesion contact) indicate that fibers may affect integrin-linked signal transduction and extracellular matrix proteins.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:85800 CAPLUS
DOCUMENT NUMBER: 132:234686
TITLE: LPP, an actin cytoskeleton protein related to zyxin, harbors a nuclear export signal and transcriptional activation capacity
AUTHOR(S): Petit, Marleen M. R.; Fradelizi, Julie; Golsteyn, Roy M.; Ayoubi, Torik A. Y.; Menichi, Bernadette; Louvard, Daniel; Van de Ven, Wim J. M.; Friederich, Evelyne
CORPORATE SOURCE: Laboratory for Molecular Oncology, Center for Human Genetics, University of Leuven and Flanders Interuniversity Institute for Biotechnology, Louvain, B-3000, Belg.
SOURCE: Molecular Biology of the Cell (2000), 11(1), 117-129
CODEN: MBCEEV; ISSN: 1059-1524
PUBLISHER: American Society for Cell Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The LPP gene is the preferred translocation partner of the HMGIC gene in a subclass of human benign mesenchymal tumors known as lipomas. Here we have characterized the LPP gene product that shares 41% of sequence identity with the focal adhesion protein zyxin. LPP localizes in focal adhesions as well as in cell-to-cell contacts, and it binds VASP, a protein implicated in the control of actin organization. In addition, LPP accumulates in the nucleus of cells upon treatment with leptomycin B, an inhibitor of the export factor CRM1. The nuclear export of LPP depends on an N-terminally located leucine-rich sequence that shares sequence homol. with well-defined nuclear export

signals. Moreover, LPP displays transcriptional activation capacity, as measured by GAL4-based assays. Altogether, these results show that the LPP protein has multifunctional domains and may serve as a scaffold upon which distinct protein complexes are assembled in the cytoplasm and in the nucleus.
REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:331285 CAPLUS
DOCUMENT NUMBER: 129:77980
TITLE: The focal adhesion phosphoprotein, VASP
AUTHOR(S): Holt, Mark R.; Critchley, David R.; Brindle, Nicholas P. J.
CORPORATE SOURCE: Department of Biochemistry, University of Leicester, Leicester, LE1 7RH, UK
SOURCE: International Journal of Biochemistry & Cell Biology (1998), 30(3), 307-311
CODEN: IJBBFU; ISSN: 1357-2725
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 14 refs. Vasodilator-stimulated phosphoprotein (VASP) is associated with focal adhesions and areas of dynamic membrane activity, where it is thought to have an important role in actin filament assembly and cell motility. VASP contains a central proline-rich sequence which recruits the G-actin binding protein profilin. Localization of VASP to the leading edge of a migrating cell can lead to local accumulation of profilin, which in turn can supply actin monomers to growing filament ends. VASP binds to the focal adhesion proteins vinculin and zyxin and this probably directs the phosphoprotein to focal adhesions and the leading edge of stimulated cells. VASP functions as a binding intermediate between profilin and focal adhesion proteins. Intracellular pathogens, including Listeria monocytogenes, have coat proteins which bind VASP. This is one way in which these pathogens use VASP, and other proteins from the host cell, to assemble the actin filaments they require to move around the cytoplasm of infected cells and enter neighboring cells. Understanding the role of VASP and other proteins in cell and bacterial motility is likely to lead to development of new therapeutic strategies for diseases including atherosclerosis and tumor growth, and for limiting the spread of intracellular pathogens.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs 8-14

L6 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:168956 CAPLUS
DOCUMENT NUMBER: 128:281277
TITLE: Down-regulated proteins of mesenchymal tumor cells
AUTHOR(S): Schenker, Thomas; Trueb, Beat
CORPORATE SOURCE: MEM-Institute, Division of Biology, University of Bern, Bern, CH-3010, Switz.
SOURCE: Experimental Cell Research (1998), 239(1), 161-168
CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To identify proteins that are lost during the establishment of the transformed phenotype of a tumor cell, the authors have prepared a subtracted cDNA library with mRNA from normal human fibroblasts and from their matched SV40 transformed counterparts. More than 40 clones were obtained that showed a dramatic reduction in their relative expression after

oncogenic transformation. The proteins encoded by these clones could be grouped into four distinct classes: extracellular matrix proteins (fibronectin, βig-h3, collagen VI), enzymes (collagenase, urokinase), cytoskeletal proteins (vinculin, SM22) and regulatory proteins (β-glycan, integrin-associated protein, myosin kinase, IGFBP-5). Six novel gene products were discovered during these expts., including a novel serine protease, a zyxin-like protein, an ankyrin-like protein, and a GTP-binding protein. Only four of all the transformation-sensitive cDNAs were consistently down-regulated when a variety of cell lines derived from spontaneous mesenchymal tumors was investigated: βig-h3, collagen VI, the novel ankyrin-like protein, and IGFBP-5. It is likely that these gene products play an important role in the maintenance of the normal phenotype.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:124880 CAPLUS
DOCUMENT NUMBER: 118:124880
TITLE: Steroid derivatives with 2-propynyloxy group in position 3, useful as intermediates for radiotherapeutics, and method of their preparation
INVENTOR(S): Pouzar, Vladimir; Schneiderova, Lenka; Drasar, Pavel; Strouf, Oldrich; Havel, Miroslav
PATENT ASSIGNEE(S): Czech.
SOURCE: Czech., 6 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 267444	B1	19900212	CS 1988-5354	19880728

PRIORITY APPLN. INFO.: CS 1988-5354 19880728
OTHER SOURCE(S): MARPAT 118:124880
AB Steroids HC.tplbond.CCH2OR [I; R = 5-cholesten-3β-yl, 20-oxo-5-pregnen-3β-yl, 17-oxo-5-androsten-3β-yl, 17β-methoxymethoxy-5-androsten-3β-yl] were prepared as intermediates for steroidal [10B]-dicarbadodecaborane derivs., used for neutron-capture therapy of hormone-dependent tumors. I were prepared in 6-32% yield by reaction of corresponding alcs. ROH with 1-5 mol equiv HC.tplbond.CCH2Br in an organic solvent (especially 2:1 C6H6/MeCN), in the presence of a quaternary ammonium salt such as Bu4NHSO4 [mol ratio 1:(1-4) vs. ROH] and aqueous 10-19M NaOH at 10-70°.

L6 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:124878 CAPLUS
DOCUMENT NUMBER: 118:124878
TITLE: Steroid derivatives with 2-propynyloxy group in position 20, useful as intermediates for radiotherapeutics, and method of their preparation
INVENTOR(S): Pouzar, Vladimir; Schneiderova, Lenka; Drasar, Pavel; Strouf, Oldrich; Havel, Miroslav
PATENT ASSIGNEE(S): Czech.
SOURCE: Czech., 5 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

CS 267443	B1	19900212	CS 1988-5353	19880728
PRIORITY APPLN. INFO.:			CS 1988-5353	19880728

OTHER SOURCE(S): MARPAT 118:124878

AB Steroids HC.tplbond.CCH2OR [I; R = 3β-methoxymethoxy-21-nor-5-pregnen-20-yl, 3-oxo-21-nor-4-pregnen-20-yl] were prepared as intermediates for steroidal [10B]-dicarbadodecaborane derivs., used for neutron-capture therapy of hormone-dependent tumors. I were prepared in 10-32% yield by reaction of corresponding alcs. ROH with 1-5 mol equiv HC.tplbond.CCH2Br in an organic solvent (especially 2:1 C6H6/MeCN), in the presence of a quaternary ammonium salt such as Bu4NHSO4 [mol ratio 1:(1-4) vs. ROH] and aqueous 10-19M NaOH at 10-70°.

L6 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1993:124876 CAPLUS

DOCUMENT NUMBER: 118:124876

TITLE: Steroid derivatives with 2-propynyloxy group in position 17, useful as intermediates for radiotherapeutics, and method of their preparation

INVENTOR(S): Pouzar, Vladimir; Schneiderova, Lenka; Drasar, Pavel; Strouf, Oldrich; Havel, Miroslav

PATENT ASSIGNEE(S): Czech.

SOURCE: Czech., 6 pp.
CODEN: CZXXA9

DOCUMENT TYPE: Patent

LANGUAGE: Czech

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 267442	B1	19900212	CS 1988-5351	19880728
PRIORITY APPLN. INFO.:			CS 1988-5351	19880728

OTHER SOURCE(S): MARPAT 118:124876

AB Steroids HC.tplbond.CCH2OR [I; R = 3-(2-tetrahydropyranyloxy)-1,3,5(10)-estratrien-17β-yl, 3β-methoxymethoxy-5-androsten-17β- or -17α-yl, 3β-(2-tetrahydropyranyloxy)-5-androsten-17β-yl, 3-oxo-4-androsten-17β-yl] were prepared as intermediates for steroidal [10B]-dicarbadodecaborane derivs., used for neutron-capture therapy of hormone-dependent tumors. I were prepared in 8-32% yield by reaction of corresponding alcs. ROH with 1-5 mol equiv HC.tplbond.CCH2Br in an organic solvent (especially 2:1 C6H6/MeCN), in the presence of a quaternary ammonium salt such as Bu4NHSO4 [mol ratio 1:(1-4) vs. ROH] and aqueous 10-19M NaOH at 10-70°.

L6 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1991:159979 CAPLUS

DOCUMENT NUMBER: 114:159979

TITLE: Potential new photosensitizers for photodynamic therapy

AUTHOR(S): Ho, Yau Kwan; Pandey, Ravindra K.; Sumlin, Adam B.; Missert, Joseph R.; Bellnier, David A.; Dougherty, Thomas J.

CORPORATE SOURCE: Oncol. Found. Buffalo, Buffalo, NY, 14203, USA

SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (1990), 1203(Proc. Photodyn. Ther.: Mech. 2, 1990), 293-300
CODEN: PSISDG; ISSN: 0277-786X

DOCUMENT TYPE: Journal

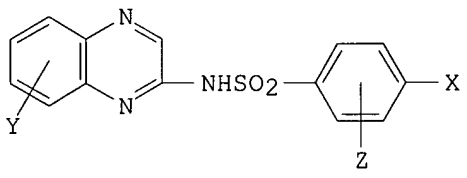
LANGUAGE: English

AB The production and tumor photosensitizing effects of 3 new photosensitizers, i.e., bis(dimethylhydroxypropylsiloxy)silicon naphthalocyanine, bis(dimethylacetoxypropylsiloxy)silicon naphthalocyanine, and especially 2-(1-O-hexyl)ethyldesvinylmethylpheophorbide a, were examined

L6 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1987:169038 CAPLUS
DOCUMENT NUMBER: 106:169038
TITLE: Quinoxaline derivatives as neoplasm inhibitors
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62000426	A	19870106	JP 1986-146277	19860624
EP 215200	A2	19870325	EP 1986-108295	19860618
EP 215200	A3	19890802		
EP 215200	B1	19920909		
R: CH, DE, FR, GB, IT, LI, NL				
CA 1267604	A1	19900410	CA 1986-511938	19860619
US 4931433	A	19900605	US 1987-45256	19870501
PRIORITY APPLN. INFO.:			US 1985-748070 A	19850624
			US 1986-858092 B1	19860429

OTHER SOURCE(S): MARPAT 106:169038
GI



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AB Quinoxaline derivs. I (Y = NO2, OMe, H, Cl, Br, OH; X = NO2, NH2, acylamido, NH(CH2)nCOOH, NHCH2SO3H; Z = H or halo), especially 2-sulfonylamino-5-chloroquinoxaline (II), are neoplasm inhibitors as determined by the Sheamaker method (1985). In vivo, II (200-449 mg/kg/day) prolonged the life span of mice transplanted with human LOX melanin-deficient melanocarcinoma.

L6 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:405881 CAPLUS
DOCUMENT NUMBER: 99:5881
TITLE: Isoprenylamine derivatives and their acid addition salts
INVENTOR(S): Tahara, Yoshiyuki; Komatsu, Yasuhiro; Koyama, Hiroyasu; Kubota, Reiko; Yamaguchi, Teruhito; Takahashi, Toshihiro
PATENT ASSIGNEE(S): Nisshin Flour Milling Co., Ltd., Japan
SOURCE: Ger. Offen., 27 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3218822	A1	19821202	DE 1982-3218822	19820518
DE 3218822	C2	19901018		
JP 57192340	A	19821126	JP 1981-76155	19810518

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     JP 01028736          B     19890605
     US 4568765           A     19860204    US 1982-377577          19820512
     GB 2098613           A     19821124    GB 1982-14242           19820517
     GB 2098613           B     19850109
     FR 2505824           A1    19821119    FR 1982-8704            19820518
     FR 2505824           B1    19860425
PRIORITY APPLN. INFO.:                       JP 1981-76155       A  19810518
OTHER SOURCE(S):         CASREACT 99:5881; MARPAT 99:5881
AB   H(CH2CRMeCHR1CH2)n[NR2(CH2)p]qNHR2 (n = 2-10; p = 2 or 3; q ≥2,
     especially 2 or 3; R, R1 = H, H or bond; R2 = H, Bz, PhCH2 or
     lower alkyl or acyl) were prepared  Thus decaprenyl bromide reacted with
     triethylenetetramine to give, via the tetrakis(trifluoroacetyl) derivative,
     H(CH2CMe:CHCH2)10(NHCH2CH2)3NH2, which provided 87.9% protection against
     Vaccinia infections and gave increased survival times in 5/6 of cases
     against KN7-8 tumor cells in mice.


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=> s ESP-2 or HED-2 or Zyxin or Zyxin-2
           381 ESP
            19 ESPS
           388 ESP
                 (ESP OR ESPS)
        380284 2
             2 ESP-2
                 (ESP(W)2)
            32 HED
             2 HEDS
            33 HED
                 (HED OR HEDS)
        380284 2
             0 HED-2
                 (HED(W)2)
            10 ZYXIN
            10 ZYXIN
        380284 2
             0 ZYXIN-2
                 (ZYXIN(W)2)
L7          12 ESP-2 OR HED-2 OR ZYXIN OR ZYXIN-2

=> s cancer? or tumor? or neoplas?
         17132 CANCER?
         14172 TUMOR?
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         2482 NEOPLAS?
L8      27419 CANCER? OR TUMOR? OR NEOPLAS?

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L9           2 L7 AND L8

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L9   ANSWER 1 OF 2  DISSABS COPYRIGHT (C) 2007 ProQuest Information and
     Learning Company; All Rights Reserved on STN
ACCESSION NUMBER:   2001:26596  DISSABS   Order Number: AAI9988630
TITLE:              Characterization of TRIP6, a new zyxin family
                    member
AUTHOR:             Yi, Jinseong [Ph.D.]; Beckerle, Mary C. [adviser]
CORPORATE SOURCE:   The University of Utah (0240)
SOURCE:             Dissertation Abstracts International, (2000) Vol. 61, No.
                    9B, p. 4521. Order No.: AAI9988630. 160 pages.
                    ISBN: 0-599-95237-7.
DOCUMENT TYPE:      Dissertation
FILE SEGMENT:       DAI
LANGUAGE:           English

L9   ANSWER 2 OF 2  DISSABS COPYRIGHT (C) 2007 ProQuest Information and
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ACCESSION NUMBER:   2000:35209  DISSABS   Order Number: AAI9956453
TITLE:              Regulation of the cytoskeleton in human microvascular
                    endothelial cells
AUTHOR:             Zimmerman, Matthew John [Ph.D.]; Feramisco, James R.
                    [adviser]
CORPORATE SOURCE:   University of California, San Diego (0033)
SOURCE:             Dissertation Abstracts International, (2000) Vol. 61, No.
                    1B, p. 52. Order No.: AAI9956453. 139 pages.
DOCUMENT TYPE:      Dissertation
FILE SEGMENT:       DAI
LANGUAGE:           English


=> s therap? or treat? or inhibit? or suppres?
        38515 THERAP?
       163294 TREAT?
        67152 INHIBIT?
        23440 SUPPRES?
L10    248978 THERAP? OR TREAT? OR INHIBIT? OR SUPPRES?

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L11          1 L9 AND L10

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L11  ANSWER 1 OF 1  DISSABS COPYRIGHT (C) 2007 ProQuest Information and
     Learning Company; All Rights Reserved on STN
ACCESSION NUMBER:   2000:35209  DISSABS   Order Number: AAI9956453
TITLE:              Regulation of the cytoskeleton in human microvascular
                    endothelial cells
AUTHOR:             Zimmerman, Matthew John [Ph.D.]; Feramisco, James R.
                    [adviser]
CORPORATE SOURCE:   University of California, San Diego (0033)
SOURCE:             Dissertation Abstracts International, (2000) Vol. 61, No.
                    1B, p. 52. Order No.: AAI9956453. 139 pages.
DOCUMENT TYPE:      Dissertation
FILE SEGMENT:       DAI
LANGUAGE:           English
AB          Angiogenesis is required for the growth of solid tumors.
     VEGF, by virtue of an expression pattern of receptors restricted mainly to
     the endothelium, is a critical regulator of angiogenesis in vivo.
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Representational difference analysis was utilized to clone genes that were upregulated in endothelial cells 2 hours after treatment with VEGF. Two genes, fra-1 and TR3, both themselves regulators of transcription, were found to be upregulated 3.1 and 1.4 fold respectively. A third gene product, zyxin, was found to localize with focal adhesions and stress fibers after

VEGF treatment, in contrast to the effects of another angiogenic factor, 12-tetradeconoylphorbol 13-acetate (TPA), which caused loss of zyxin localization to these structures. Loss of zyxin at stress fibers and focal adhesions over time and dose of TPA treatment correlated with a reduced electrophoretic mobility of zyxin on polyacrylamide gels which was determined to be due to phosphorylation of the protein. Both effects were blocked by inhibition of PKC activity. Inhibition of MEK activity, however, inhibited zyxin phosphorylation downstream of TPA treatment, but not loss of zyxin at focal adhesions and stress fibers, indicating that zyxin phosphorylation could be decoupled from the cytoskeletal rearrangements induced by TPA. Introduction of inactivated cdc42 into HMvECs paralleled the effect of VEGF increased localization of zyxin to actin stress fibers and focal adhesions, an effect which may be mediated by the inactivation of the downstream effector PAK. Inactivation of PAK alone and in combination with activated cdc42 increased stress fiber formation in HMvECs, supporting the hypothesis that PAK mediates stress fiber breakdown. However, PAK inactivation is also predicted to inhibit LIM-kinase, and inhibition of LIM-kinase by independent means inhibited, not cooperated with, the phenotype induced by activated cdc42. These apparently contradictory results my be explained by alternate emerging regulatory pathways.

AB Angiogenesis is required for the growth of solid tumors. VEGF, by virtue of an expression pattern of receptors restricted mainly to the endothelium, is a critical regulator of angiogenesis in vivo. Representational difference analysis was utilized to clone genes that were upregulated in endothelial cells 2 hours after treatment with VEGF. Two genes, fra-1 and TR3, both themselves regulators of transcription, were found to be upregulated 3.1 and 1.4 fold respectively. A third gene product, zyxin, was found to localize with focal adhesions and stress fibers after

VEGF treatment, in contrast to the effects of another angiogenic factor, 12-tetradeconoylphorbol 13-acetate (TPA), which caused loss of zyxin localization to these structures. Loss of zyxin at stress fibers and focal adhesions over time and dose of TPA treatment correlated with a reduced electrophoretic mobility of zyxin on polyacrylamide gels which was determined to be due to phosphorylation of the protein. Both effects were blocked by inhibition of PKC activity. Inhibition of MEK activity, however, inhibited zyxin phosphorylation downstream of TPA treatment, but not loss of zyxin at focal adhesions and stress fibers, indicating that zyxin phosphorylation could be decoupled from the cytoskeletal rearrangements induced by TPA. Introduction of inactivated cdc42 into HMvECs paralleled the effect of VEGF increased localization of zyxin to actin stress fibers and focal adhesions, an effect which may be mediated by the inactivation of the downstream effector. . . fiber formation in HMvECs, supporting the hypothesis that PAK mediates stress fiber breakdown. However, PAK inactivation is also predicted to inhibit LIM-kinase, and inhibition of LIM-kinase by independent means inhibited, not cooperated with, the phenotype induced by activated cdc42. These apparently contradictory results my be explained by alternate emerging regulatory. . .

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